### STEP THERAPY CRITERIA

<table>
<thead>
<tr>
<th>DRUG CLASS*</th>
<th>ACNE PRODUCTS TOPICAL (BRAND ONLY)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRAND NAME</td>
<td>(generic)</td>
</tr>
<tr>
<td>ACZONE</td>
<td>(dapsone)</td>
</tr>
<tr>
<td>ACANYA</td>
<td>(clindamycin phosphate-benzoyl peroxide)</td>
</tr>
<tr>
<td>BENZACLIN</td>
<td>(clindamycin phosphate-benzoyl peroxide)</td>
</tr>
<tr>
<td>CLEOCIN-T</td>
<td>(clindamycin phosphate)</td>
</tr>
<tr>
<td>CLINDACIN ETZ</td>
<td>(clindamycin phosphate)</td>
</tr>
<tr>
<td>CLINDACIN PAC</td>
<td>(clindamycin phosphate)</td>
</tr>
<tr>
<td>CLINDACIN-P</td>
<td>(clindamycin phosphate)</td>
</tr>
<tr>
<td>CLINDAGEL</td>
<td>(clindamycin phosphate)</td>
</tr>
<tr>
<td>DUAC</td>
<td>(clindamycin phosphate-benzoyl peroxide)</td>
</tr>
<tr>
<td>EVOCLIN</td>
<td>(clindamycin phosphate)</td>
</tr>
<tr>
<td>KLARON</td>
<td>(sulfacetamide sodium)</td>
</tr>
<tr>
<td>NEUAC</td>
<td>(clindamycin phosphate-benzoyl peroxide)</td>
</tr>
</tbody>
</table>

*Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

**Status:** CVS Caremark Criteria  
**Type:** Initial Step Therapy; Post Step Therapy Prior Authorization  
**Ref # 1493-D**
FDA-APPROVED INDICATIONS

Aczone
Aczone is indicated for the topical treatment of acne vulgaris.

Acanya
Acanya is indicated for the topical treatment of acne vulgaris in patients 12 years or older.

BenzaClin
BenzaClin is indicated for the topical treatment of acne vulgaris.

Clindamycin Phosphate
Clindamycin phosphate products are indicated in the treatment of acne vulgaris. In view of the potential for diarrhea, bloody diarrhea and pseudomembranous colitis, the physician should consider whether other agents are more appropriate.

Duac
Duac (clindamycin phosphate and benzoyl peroxide) is indicated for the topical treatment of inflammatory acne vulgaris in patients 12 years and older.

Limitations of Use
Duac has not been demonstrated to have any additional benefit when compared with benzoyl peroxide alone in the same vehicle when used for the treatment of non-inflammatory acne.

Klaron
Klaron is indicated in the topical treatment of acne vulgaris.

Neuac
Neuac (clindamycin phosphate and benzoyl peroxide is indicated for the topical treatment of inflammatory acne vulgaris.

Limitations of Use
Neuac has not been demonstrated to have any additional benefit when compared with benzoyl peroxide alone in the same vehicle when used for the treatment of non-inflammatory acne.

INITIAL STEP THERAPY
If the patient has filled a prescription for at least a 30 day supply of a generic acne product (benzoyl peroxide, clindamycin topical, clindamycin/benzoyl peroxide, erythromycin topical, erythromycin/benzoyl peroxide, sodium sulfacetamide, or sodium sulfacetamide/sulfur) within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for acne vulgaris.
- The patient has demonstrated an inadequate treatment response or intolerance to a generic acne product.

RATIONALE
If the patient has filled a prescription for at least a 30 day supply of a generic acne product (benzoyl peroxide, clindamycin topical, clindamycin/benzoyl peroxide, erythromycin topical, erythromycin/benzoyl peroxide, sodium sulfacetamide, or sodium sulfacetamide/sulfur) within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested branded drug will be paid under that prescription benefit.
If the patient does not meet the initial step therapy criteria, then prior authorization is required.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Aczone, Acanya, BenzaClin, Clindamycin Phosphate, Duac, Klaron, and Neuac are indicated for the topical treatment of acne vulgaris. Acanya and Duac are only indicated in patients 12 years and older. Duac and Neuac are indicated specifically for inflammatory acne vulgaris.

If the patient has demonstrated an inadequate treatment response or intolerance to a topical generic acne product and the requested drug is being prescribed for acne vulgaris, then the requested brand drug will be approved.

REFERENCES

Written by: UM Development (CF)
Date Written: 06/2016
Revised: (SF) 06/2017 (no clinical changes), 06/2018 (no clinical changes), (ME) 06/2019 (removed Clindamax)
Reviewed: Medical Affairs: (GAD) 06/2016
External Review: 10/2016, 10/2017, 10/2018, 10/2019

CRITERIA FOR APPROVAL

<p>| | |</p>
<table>
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<tr>
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<tbody>
<tr>
<td>1</td>
<td>Is the requested drug being prescribed for acne vulgaris?</td>
</tr>
<tr>
<td>2</td>
<td>Has the patient experienced an inadequate treatment response or intolerance to a topical generic acne product?</td>
</tr>
</tbody>
</table>

Mapping Instructions

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Go to 2</td>
<td>Deny</td>
</tr>
<tr>
<td></td>
<td>You do not meet the requirements of your plan.</td>
</tr>
<tr>
<td></td>
<td>Your plan covers this drug when you have acne vulgaris.</td>
</tr>
<tr>
<td></td>
<td>Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]</td>
</tr>
</tbody>
</table>

| 2. Approve, 12 months | Deny |
|   | You do not meet the requirements of your plan. |
|   | Your plan covers this drug when you have tried a topical generic acne product and it did not work for you. |
|   | Your request has been denied based on the information we have. [Short description: No inadequate treatment response or intolerance to |
topical generic acne products
SPECIALTY GUIDELINE MANAGEMENT

ACTEMRA (tocilizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Moderately to severely active rheumatoid arthritis
   2. Active polyarticular juvenile idiopathic arthritis
   3. Active systemic juvenile idiopathic arthritis
   4. Giant cell arteritis

B. Compendial Uses
   1. Unicentric Castleman’s disease
   2. Multicentric Castleman’s disease
   3. Refractory/severe immunotherapy-related inflammatory arthritis not responding to corticosteroids and anti-inflammatory agents

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active rheumatoid arthritis (RA)
   1. Authorization of 24 months may be granted for members who have previously received Actemra or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) indicated for moderately to severely active rheumatoid arthritis.
   2. Authorization of 24 months may be granted for treatment of moderately to severely active RA when any of the following criteria is met:
      a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
      b. Member has an intolerance or contraindication to methotrexate (see Appendix).

B. Active Polyarticular Juvenile Idiopathic Arthritis (pJIA)
   Authorization of 24 months may be granted for members who have previously received Actemra or Orencia.

   Authorization of 24 months may be granted for treatment of active pJIA when any of the following criteria is met:
   1. Member has experienced an inadequate response to at least a 3-month trial of a TNF inhibitor (e.g., Enbrel, Humira, or Remicade).
   2. Member has experienced an intolerance or has contraindication to a TNF inhibitor.
C. **Active Systemic Juvenile Idiopathic Arthritis (sJIA)**
   Authorization of 24 months may be granted for members who have previously received Actemra or Kineret.

   Authorization of 24 months may be granted for treatment of active sJIA when any of the following criteria is met:
   1. Member has an inadequate response to at least a 2-week trial of corticosteroids.
   2. Member has an inadequate response to at least a 3-month trial of methotrexate or leflunomide.

D. **Giant Cell Arteritis**
   Authorization of 12 months may be granted for treatment of giant cell arteritis.

E. **Unicentric and Multicentric Castleman’s Disease**
   Authorization of 12 months may be granted for treatment of unicentric or multicentric Castleman’s disease.

F. **Immunotherapy-related Inflammatory Arthritis**
   Authorization of 12 months may be granted for treatment of severe/refractory immunotherapy-related inflammatory arthritis that is not responding to corticosteroids and anti-inflammatory agents.

III. **CONTINUATION OF THERAPY**

A. **Rheumatoid Arthritis, Polyarticular Juvenile Idiopathic Arthritis and Systemic Juvenile Idiopathic Arthritis**
   Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Actemra as evidenced by low disease activity or improvement in signs and symptoms of the condition.

B. **All Other Diagnoses**
   All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. **OTHER**

   For all indications: Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB)

   Note: Members who have received Actemra or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) are exempt from requirements related to TB screening in this Policy.

V. **APPENDIX: Examples of Contraindications to Methotrexate**
   1. Alcoholism, alcoholic liver disease or other chronic liver disease
   2. Breastfeeding
   3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
   4. Elevated liver transaminases
   5. History of intolerance or adverse event
   6. Hypersensitivity
   7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
   8. Myelodysplasia
   9. Pregnancy or planning pregnancy (male or female)
10. Renal impairment
11. Significant drug interaction

VI. REFERENCES
INDICATION- SPECIFIC SPECIALTY GUIDELINE MANAGEMENT

H.P. ACTHAR GEL (repository corticotropin injection)

POLICY

I. INDICATIONS

The indication-specific Specialty Guideline Management (SGM) program provides coverage for specific, but not all FDA labeled or compendial supported drug use based on plan design and the scope of the pharmacy benefit. This program provides coverage for H.P. Acthar Gel for the treatment of infantile spasms and exacerbations of multiple sclerosis if all of the approval criteria are met.

A. Infantile spasms: as monotherapy for the treatment of infantile spasms in infants and children under 2 years of age
B. Multiple Sclerosis: treatment of acute exacerbations of multiple sclerosis in adults

The use of H.P. Acthar for the treatment of all other indications listed in the FDA product labeling has not been proven to be superior to conventional therapies (e.g., corticosteroids, immunosuppressive agents) and has a significantly higher cost than the standard of care agents. Use of H. P. Acthar for these conditions is considered not medically necessary and is not a covered benefit.

A. Rheumatic Disorders: as adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in: psoriatic arthritis; rheumatoid arthritis, including juvenile rheumatoid arthritis, ankylosing spondylitis
B. Collagen Diseases: during an exacerbation or as maintenance therapy in selected cases of: systemic lupus erythematosus, systemic dermatomyositis (polymyositis)
C. Dermatologic Diseases: severe erythema multiforme, Stevens-Johnson syndrome
D. Allergic States: serum sickness
E. Ophthalmic Diseases: severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as: keratitis, iritis, iridocyclitis, diffuse posterior uveitis and choroiditis, optic neuritis, chorioretinitis, anterior segment inflammation
F. Respiratory Diseases: symptomatic sarcoidosis
G. Edematous State: to induce a diuresis or a remission of proteinuria in the nephrotic syndrome without uremia of the idiopathic type or that due to lupus erythematosus

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review for requests for treatment of multiple sclerosis exacerbations: chart notes detailing the outcomes of the most recent trial with IV methylprednisolone, including dosage and duration of treatment.

III. CRITERIA FOR INITIAL APPROVAL

A. Infantile Spasms

Authorization of 4 weeks may be granted for treatment of infantile spasms in members who are less than 2 years of age.
B. Multiple Sclerosis
Authorization of 3 weeks may be granted for treatment of acute exacerbations of multiple sclerosis when the member has had an inadequate response to a trial of IV methylprednisolone (for the current exacerbation).

IV. CONTINUATION OF THERAPY
A. Infantile Spasms
Authorization of 4 weeks may be granted to members requesting H.P. Acthar Gel for continuation of therapy when the member has shown substantial clinical benefit from therapy.

B. Multiple sclerosis
Authorization of 3 weeks may be granted for members requesting re-authorization for H.P. Acthar therapy when all initial authorization criteria are met.

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

H.P. ACTHAR GEL (repository corticotropin injection)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. **Infantile spasms**: as monotherapy for the treatment of infantile spasms in infants and children under 2 years of age

2. **Multiple Sclerosis**: treatment of acute exacerbations of multiple sclerosis in adults

3. **Rheumatic Disorders**: as adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in: psoriatic arthritis; rheumatoid arthritis, including juvenile rheumatoid arthritis, ankylosing spondylitis

4. **Collagen Diseases**: during an exacerbation or as maintenance therapy in selected cases of: systemic lupus erythematosus, systemic dermatomyositis (polymyositis)

5. **Dermatologic Diseases**: severe erythema multiforme, Stevens-Johnson syndrome

6. **Allergic States**: serum sickness

7. **Ophthalmic Diseases**: severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as: keratitis, iritis, iridocyclitis, diffuse posterior uveitis and choroiditis, optic neuritis, chorioretinitis, anterior segment inflammation

8. **Respiratory Diseases**: symptomatic sarcoidosis

9. **Edematous State**: to induce a diuresis or a remission of proteinuria in the nephrotic syndrome without uremia of the idiopathic type or that due to lupus erythematosus

B. Compendial Use: Diagnostic testing of adrenocortical function

All other indications are considered experimental/investigational and are not covered benefits.

II. CRITERIA FOR INITIAL APPROVAL

A. **Infantile Spasms**

Authorization of 6 months may be granted for treatment of infantile spasms in members who are less than 2 years of age.

B. **Multiple Sclerosis**

Authorization of 3 weeks may be granted for treatment of acute exacerbations of multiple sclerosis when the member has had an inadequate response to a trial of parenteral or oral glucocorticoids.

C. **Nephrotic Syndrome**

Authorization of 3 months may be granted for treatment of nephrotic syndrome when H.P. Acthar Gel is requested for induction of diuresis or for remission of proteinuria in a member who has had an inadequate response to a trial of parenteral or oral glucocorticoids.
D. Rheumatic Disorders
Authorization of 3 months may be granted to members who are prescribed H.P. Acthar Gel as adjunctive treatment for rheumatic disorders (e.g., psoriatic arthritis, rheumatoid arthritis, ankylosing spondylitis) when the member has had an inadequate response to a trial of parenteral or oral glucocorticoids.

E. Collagen Diseases
Authorization of 3 months may be granted for treatment of collagen diseases (e.g., systemic lupus erythematosus, systemic dermatomyositis, polymyositis) when the member has had an inadequate response to a trial of parenteral or oral glucocorticoids.

F. Dermatologic Diseases
Authorization of 3 months may be granted for treatment of dermatologic disorders (e.g., severe erythema multiforme, Stevens-Johnson syndrome) when the member has had an inadequate response to a trial of parenteral or oral glucocorticoids.

G. Ophthalmic Diseases
Authorization of 3 months may be granted for treatment of ophthalmic diseases (e.g., keratitis, iritis, iridocyclitis, diffuse posterior uveitis and choroiditis, optic neuritis, chorioretinitis, anterior segment inflammation) when the member has had an inadequate response to a trial of parenteral, oral, or topical ophthalmic glucocorticoids.

H. Symptomatic Sarcoidosis
Authorization of 3 months may be granted to for treatment of symptomatic sarcoidosis when the member has had an inadequate response to a trial of parenteral or oral glucocorticoids.

I. Serum Sickness
Authorization of 1 month may be granted for treatment of serum sickness when the member has had an inadequate response to a trial of parenteral or oral glucocorticoids.

J. Diagnostic Testing of Adrenocortical Function
Authorization of 1 dose may be granted to members who are prescribed H.P. Acthar Gel for diagnostic testing of adrenocortical function when member cannot be tested with Cosyntropin.

III. CONTINUATION OF THERAPY

A. Infantile Spasms
Authorization of 6 months may be granted to members requesting H.P. Acthar Gel for continuation of therapy when the member has shown substantial clinical benefit from therapy.

B. All Other Indications
All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

ACTIMMUNE (interferon gamma-1b)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Actimmune is indicated for reducing the frequency and severity of serious infections associated with chronic granulomatous disease (CGD).
   2. Actimmune is indicated for delaying time to disease progression in patients with severe, malignant osteopetrosis (SMO).

B. Compendial Uses
   1. Mycosis fungoides/Sezary syndrome
   2. Atopic dermatitis

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Chronic Granulomatous Disease
   Authorization of 12 months may be granted for the treatment of chronic granulomatous disease.

B. Severe, Malignant Osteopetrosis
   Authorization of 12 months may be granted for treatment of severe, malignant osteopetrosis.

C. Mycosis Fungoides/Sezary Syndrome
   Authorization of 12 months may be granted for the treatment of mycosis fungoides or Sezary syndrome.

D. Atopic Dermatitis
   Authorization of 12 months may be granted for the treatment of atopic dermatitis.

III. CONTINUATION OF THERAPY

Authorization of 12 months will be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.
IV. REFERENCES

### PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>BRAND NAME* (generic)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CARAC (fluorouracil)</td>
</tr>
<tr>
<td>FLUOROPLEX (fluorouracil)</td>
</tr>
<tr>
<td>PICATO (ingenol mebutate)</td>
</tr>
<tr>
<td>TOLAK (fluorouracil)</td>
</tr>
<tr>
<td>ZYCLARA (imiquimod)</td>
</tr>
</tbody>
</table>

**Status:** CVS Caremark Criteria  
**Type:** Initial Prior Authorization  
Ref # 1378-A

*Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

### FDA-APPROVED INDICATIONS

**Carac**  
Carac is indicated for the topical treatment of multiple actinic or solar keratoses of the face and anterior scalp.

**Fluoroplex**  
Fluoroplex cream is indicated for the topical treatment of multiple actinic (solar) keratoses.

**Picato**  
Picato gel is indicated for the topical treatment of actinic keratosis.

**Tolak**  
Tolak cream is indicated for the topical treatment of actinic keratosis lesions of the face, ears and/or scalp.

**Zyclara**  
**Actinic Keratosis**  
Zyclara Cream, 2.5% and 3.75% are indicated for the topical treatment of clinically typical visible or palpable, actinic keratoses (AK), of the full face or balding scalp in immunocompetent adults.

**External Genital Warts**  
Zyclara Cream, 3.75% is indicated for the treatment of external genital and perianal warts (EGW)/condyloma acuminata in patients 12 years or older.

### COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:
- The patient has the diagnosis of actinic keratosis or external genital warts
Rationale

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Carac is indicated for the topical treatment of multiple actinic or solar keratoses of the face and anterior scalp. Fluoroplex cream is indicated for is indicated for the topical treatment of multiple actinic (solar) keratoses. Tolak cream is indicated for the topical treatment of actinic keratosis lesions of the face, ears and/or scalp. Picato gel is indicated for the topical treatment of actinic keratosis. Zyclara cream is indicated for actinic keratosis and external genital warts.

References


Criteria For Approval

1. Does the patient have the diagnosis of actinic keratosis or external genital warts?
   - Yes
   - No

Guidelines For Approval

<table>
<thead>
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<th>Duration of Approval</th>
<th>12 Months</th>
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<td>Set 1</td>
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<tr>
<td>Yes to question(s)</td>
<td>No to question(s)</td>
</tr>
<tr>
<td>1</td>
<td>None</td>
</tr>
</tbody>
</table>

Mapping Instructions

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Approve, 12 months</td>
<td>Deny</td>
</tr>
</tbody>
</table>

Denial Reasons – Do Not Use For Medicare Part D

You do not meet the requirements of your plan.
Your plan covers this drug when you have actinic keratosis or external genital warts.
Your request has been denied based on the information we have.
[Short Description: No approvable diagnosis]
SPECIALTY GUIDELINE MANAGEMENT

ADAGEN (pegademase bovine) injection

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Adagen is indicated for enzyme replacement therapy for adenosine deaminase (ADA) deficiency in patients with severe combined immunodeficiency disease (SCID) who are not suitable candidates for—or who have failed—bone marrow transplantation. Adagen is recommended for use in infants from birth or in children of any age at the time of diagnosis.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of indefinite approval may be granted for treatment of severe combined immunodeficiency disease (SCID) associated with adenosine deaminase (ADA) deficiency when the condition has failed to respond to a bone marrow transplant (BMT) or the member is not currently a suitable candidate for BMT.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCE

SPECIALTY GUIDELINE MANAGEMENT

ADCETRIS (brentuximab vedotin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Classical Hodgkin Lymphoma (CHL)
   i. Treatment of CHL after failure of autologous hematopoietic stem cell transplantation (auto-HSCT) or after failure of at least two prior multi-agent chemotherapy regimens in patients who are not auto-HSCT candidates
   ii. Treatment of CHL at high risk of relapse or progression as post-auto-HSCT consolidation
   iii. Previously untreated Stage III or IV classical Hodgkin lymphoma (CHL), in combination with doxorubicin, vinblastine, and dacarbazine

2. Systemic anaplastic large cell lymphoma (sALCL)
   a. Treatment of systemic anaplastic large cell lymphoma (sALCL) after failure of at least one prior multi-agent chemotherapy regimen
   b. Previously untreated systemic anaplastic large cell lymphoma (sALCL) or other CD30-expressing peripheral T-cell lymphomas (PTCL), including angioimmunoblastic T-cell lymphoma and PTCL not otherwise specified, in combination with cyclophosphamide, doxorubicin, and prednisone

3. Treatment of primary cutaneous anaplastic large cell lymphoma (pcALCL) or CD30-expressing mycosis fungoides (MF) in patients who have received prior systemic therapy

B. Compendial Uses

   Non-Hodgkin’s Lymphoma (NHL)
   1. CD30+ adult T-cell leukemia/lymphoma
   2. Breast implant-associated anaplastic large cell lymphoma (ALCL)
   3. Mycosis Fungoides (MF)/Sezary Syndrome (SS)
   4. Lymphomatoid papulosis (LyP)
   5. CD30+ peripheral T-cell lymphoma (PTCL)
   6. CD30+ angioimmunoblastic T-cell lymphoma
   7. Diffuse large B-cell lymphoma
   8. Extranodal NK/T-cell Lymphoma (nasal type)
   9. Hepatosplenic gamma-delta T-cell lymphoma
   10. Histologic transformation of follicular lymphoma to diffuse large B-cell lymphoma
   11. Histologic transformation of marginal zone lymphoma to diffuse large B-Cell lymphoma
   12. High-grade B-Cell lymphomas
   13. AIDS-related B-Cell lymphomas
   14. Post-transplant lymphoproliferative disorders

All other indications are considered experimental/investigational and are not a covered benefit.
II. DOCUMENTATION

Testing or analysis confirming CD30 expression on the surface of the cell (initial requests).

III. CRITERIA FOR INITIAL APPROVAL

A. Classical Hodgkin lymphoma (CHL)

Authorization of 12 months may be granted for treatment of CHL when any of the following are met:

1. Adcetris will be used as a single agent, or
2. Adcetris will be used in combination with doxorubicin, vinblastine, and dacarbazine, or
3. Adcetris will be used in combination with bendamustine, or
4. Adcetris will be used in combination with dacarbazine.

B. Non-Hodgkin’s lymphoma (NHL)

Authorization of 12 months may be granted for treatment of NHL with any of the following subtypes:

1. CD30+ adult T-cell leukemia/lymphoma when either of the following are met:
   a. Adcetris will be used as a single agent, or
   b. Adcetris will be used in combination with cyclophosphamide, doxorubicin, and prednisone.

2. Systemic anaplastic large cell lymphoma when either of the following are met:
   a. Adcetris will be used as a single agent, or
   b. Adcetris will be used in combination the cyclophosphamide, doxorubicin, and prednisone (CHP).

3. Cutaneous anaplastic large cell lymphoma when either of the following are met:
   a. Adcetris will be used as a single agent, or
   b. Adcetris will be used in combination with cyclophosphamide, doxorubicin, and prednisone.

4. Breast implant associated anaplastic large cell lymphoma (ALCL) when either of the following are met:
   a. Adcetris will be used as a single agent, or
   b. Adcetris will be used in combination with cyclophosphamide, doxorubicin, and prednisone.

5. Mycosis fungoides (MF)/Sezary syndrome (SS)

6. Lymphomatoid papulosis (LyP) when both of the following are met:
   a. Adcetris will be used as a single agent, and
   b. The disease is relapsed or refractory.

7. CD30+ peripheral T-cell lymphoma (PTCL) when either of the following are met:
   a. Adcetris will be used as a single agent, or
   b. Adcetris will be used in combination with cyclophosphamide, doxorubicin, and prednisone.

8. CD30+ angioimmunoblastic T-cell lymphoma when both of the following are met:
   a. Adcetris will be used as a single agent, or
   b. Adcetris will be used in combination with cyclophosphamide, doxorubicin, and prednisone.

9. Diffuse large B-cell lymphoma when both of the following are met:
   a. Adcetris will be used as second-line or subsequent therapy, and
   b. The patient is not a candidate for transplant.

10. Extranasal NK/T-cell lymphoma (nasal type) when all of the following are met:
    a. Adcetris will be used as a single agent, and
    b. Patient has relapsed or refractory disease, and
    c. Patient has had an inadequate response or contraindication to asparaginase-based therapy (e.g., pegaspargase).

11. Hepatosplenic gamma-delta T-cell lymphoma when either of the following are met:
    a. Adcetris will be used as a single agent after two or more previous lines of chemotherapy, or
    b. Adcetris will be used in combination with cyclophosphamide, doxorubicin, and prednisone.

12. Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma when the patient has received at least two chemoimmunotherapy regimens.

13. High-grade B-cell lymphomas when both of the following are met:
   a. Adcetris will be used for second-line or subsequent therapy, and
b. The patient is not a candidate for transplant.
14. AIDS-Related B-cell lymphomas when both of the following are met:
   a. Adcetris will be used for second-line or subsequent therapy, and
   b. The patient is not a candidate for transplant.
15. Post-transplant lymphoproliferative disorders when used for second-line or subsequent therapy.
16. Histologic transformation of follicular lymphoma to diffuse large B-cell lymphoma when the patient has received at least two chemoimmunotherapy regimens.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

Adempas (riociguat)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
A. Pulmonary Arterial Hypertension (PAH)
   Adempas is indicated for the treatment of adults with pulmonary arterial hypertension (PAH), (World Health Organization [WHO] Group 1), to improve exercise capacity, WHO functional class and to delay clinical worsening.
B. Chronic Thromboembolic Pulmonary Hypertension (CTEPH)
   Adempas is indicated for the treatment of adults with persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH), (WHO Group 4) after surgical treatment, or inoperable CTEPH, to improve exercise capacity and WHO functional class.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Pulmonary Arterial Hypertension (PAH)
   Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:
   1. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (Refer to Appendix)
   2. PAH was confirmed by right heart catheterization with all of the following pretreatment results:
      i. mPAP ≥ 25 mmHg
      ii. PCWP ≤ 15 mmHg
      iii. PVR > 3 Wood units

B. Chronic Thromboembolic Pulmonary Hypertension (CTEPH)
   Authorization of 12 months may be granted for treatment of CTEPH when ALL of the following criteria are met:
   1. Member has CTEPH defined as WHO Group 4 class of pulmonary hypertension (Refer to Appendix)
   2. Member meets either criterion (i) or criterion (ii) below:
      i. Recurrent or persistent CTEPH after pulmonary endarterectomy (PEA)
      ii. Inoperable CTEPH with diagnosis confirmed by BOTH of the following (a. and b.):
         a. Computed tomography (CT)/magnetic resonance imaging (MRI) angiography or pulmonary angiography
         b. Pretreatment right heart catheterization with all of the following results:
            • mPAP ≥ 25 mmHg
            • PCWP ≤ 15 mmHg
            • PVR > 3 Wood units
III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section II who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. APPENDIX

WHO Classification of Pulmonary Hypertension

1 PAH
1.1 Idiopathic (PAH)
1.2 Heritable PAH
1.3 Drug- and toxin-induced PAH
1.4. PAH associated with:
   1.4.1 Connective tissue diseases
   1.4.2 HIV infection
   1.4.3 Portal hypertension
   1.4.4 Congenital heart diseases
   1.4.5 Schistosomiasis
1.5 PAH long-term responders to calcium channel blockers
1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease
2.1 PH due to heart failure with preserved LVEF
2.2 PH due to heart failure with reduced LVEF
2.3 Valvular heart disease
2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia
3.1 Obstructive lung disease
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction
4.1 Chronic thromboembolic PH
4.2 Other pulmonary artery obstructions
   4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
   4.2.2 Other malignant tumors
   Renal carcinoma
   Uterine carcinoma
   Germ cell tumours of the testis
   Other tumours
   4.2.3 Non-malignant tumours
   Uterine leiomyoma
   4.2.4 Arteritis without connective tissue disease
   4.2.5 Congenital pulmonary artery stenosis
   4.2.6 Parasites
   Hydatidosis

5 PH with unclear and/or multifactorial mechanisms
5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
5.4 Complex congenital heart disease

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

AFINITOR (everolimus)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Hormone Receptor-Positive, HER2-Negative Breast Cancer
   Afinitor is indicated for the treatment of postmenopausal women with advanced hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer in combination with exemestane, after failure of treatment with letrozole or anastrozole.

2. Neuroendocrine Tumors (NET)
   a. Afinitor is indicated for the treatment of adult patients with progressive neuroendocrine tumors of pancreatic origin (PNET) with unresectable, locally advanced or metastatic disease.
   b. Afinitor is indicated for the treatment of adult patients with progressive, well-differentiated, non-functional neuroendocrine tumors (NET) of gastrointestinal (GI) or lung origin with unresectable, locally advanced or metastatic disease.

3. Renal Cell Carcinoma (RCC)
   Afinitor is indicated for the treatment of adult patients with advanced renal cell carcinoma (RCC) after failure of treatment with sunitinib or sorafenib.

4. Tuberous Sclerosis Complex (TSC)-Associated Renal Angiomyolipoma
   Afinitor is indicated for the treatment of adult patients with renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery.

5. Tuberous Sclerosis Complex (TSC)-Associated Subependymal Giant Cell Astrocytoma (SEGA)
   Afinitor and Afinitor Disperz are indicated in adult and pediatric patients aged 1 year and older with tuberous sclerosis complex (TSC) for the treatment of subependymal giant cell astrocytoma (SEGA) that requires therapeutic intervention but cannot be curatively resected.

6. Tuberous Sclerosis Complex (TSC)-Associated Partial-Onset Seizures
   Afinitor Disperz is indicated for the adjunctive treatment of adult and pediatric patients aged 2 years and older with TSC-associated partial-onset seizures.

B. Compendial Uses

1. Relapsed or stage IV renal cell carcinoma:
   a. Single agent or in combination with lenvatinib as subsequent therapy for clear cell histology
   b. Single-agent systemic therapy for non-clear histology
   c. In combination with lenvatinib as systemic therapy for non-clear cell histology
   d. In combination with bevacizumab as systemic therapy for non-clear cell histology

2. Soft tissue sarcoma subtypes:
   a. Perivascular epithelioid cell tumors (PEComa), single-agent therapy
   b. Recurrent angiomylipoma, single-agent therapy
   c. Lymphangioleiomyomatosis, single-agent therapy

3. Gastrointestinal stromal tumors (GIST), in combination with either imatinib, sunitinib, or regorafenib for disease progression after single-agent therapy with imatinib, sunitinib, and regorafenib

4. Neuroendocrine tumors of the gastrointestinal tract, lung and thymus (carcinoid tumors)

5. Neuroendocrine tumors of the pancreas, single-agent therapy
6. Thymomas and thymic carcinomas, second-line therapy as a single agent
7. Classic Hodgkin lymphoma, third-line or subsequent systemic therapy as a single agent for relapsed or refractory disease
8. Central nervous system cancers:
   a. Meningiomas
   b. Glioma
   c. Subependymal giant cell astrocytoma (SEGA); adjuvant treatment as a single agent
9. Thyroid carcinoma (papillary carcinoma, Hürthle cell carcinoma, and follicular carcinoma), if clinical trials or other systemic therapies are not available or appropriate for treatment of progressive and/or symptomatic iodine-refractory
10. Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma, single-agent therapy for previously treated disease that does not respond to primary therapy or for progressive or relapsed disease
11. Endometrial carcinoma, in combination with letrozole or as adjuvant treatment for surgically staged patients in combination with letrozole
12. Invasive breast cancer
   Recurrent or stage IV (M1) hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer with no visceral crisis in postmenopausal women treated with prior endocrine therapy within 1 year or in premenopausal women treated with ovarian ablation-suppression treated with prior endocrine therapy within 1 year in combination with exemestane, fulvestrant, or tamoxifen.
13. Tuberous sclerosis complex

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Breast Cancer
   Authorization of 12 months may be granted for treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative recurrent or metastatic breast cancer when prescribed in combination with exemestane, fulvestrant, or tamoxifen and the member has received endocrine therapy within 1 year.

B. Renal Cell Carcinoma
   Authorization of 12 months may be granted for treatment of relapsed or metastatic RCC when any of the following criteria are met:
   1. Afinitor is given as a single agent or in combination with lenvatinib as subsequent therapy for clear cell histology; OR
   2. Afinitor is given as single-agent systemic therapy for non-clear cell histology; OR
   3. Afinitor is given in combination with lenvatinib as systemic therapy for non-clear cell histology; OR
   4. Afinitor is given in combination with bevacizumab as systemic therapy for non-clear cell histology.

C. Neuroendocrine Tumors
   1. Authorization of 12 months may be granted for treatment of progressive neuroendocrine tumors (PNET) of pancreatic origin in members with unresectable, locally advanced, or metastatic disease.
   2. Authorization of 12 months may be granted for treatment of progressive, well-differentiated, non-functional neuroendocrine tumors (NET) of gastrointestinal, lung, or thymic origin with unresectable, locally advanced or metastatic disease.

D. Tuberous Sclerosis Complex (TSC)
Authorization of 12 months may be granted for treatment of TSC.

E. Soft Tissue Sarcoma
Authorization of 12 months may be granted for treatment of any of the following subtypes of soft tissue sarcoma as single agent therapy: perivascular epithelioid cell (PEComa), recurrent angiomyolipoma, or lymphangioleiomyomatosis.

F. Gastrointestinal Stromal Tumor (GIST)
Authorization of 12 months may be granted for treatment of gastrointestinal stromal tumors in combination with either imatinib, sunitinib, or regorafenib for disease progression after single-agent therapy with imatinib, sunitinib, and regorafenib.

G. Thymoma and Thymic Carcinoma
Authorization of 12 months may be granted for treatment of thymoma or thymic carcinoma for second-line therapy as a single agent.

H. Classic Hodgkin Lymphoma
Authorization of 12 months may be granted for treatment of relapsed or refractory classic Hodgkin lymphoma for third-line or subsequent systemic therapy as a single agent.

I. Waldenström’s Macroglobulinemia/Lymphoplasmacytic Lymphoma
Authorization of 12 months may be granted for treatment of Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma as a single-agent therapy for previously treated disease that does not respond to primary therapy or for progressive relapsed disease.

J. Thyroid Carcinoma
Authorization of 12 months may be granted for treatment of progressive and/or symptomatic iodine-refractory thyroid carcinoma with any of the following histologies: papillary, Hurthle cell, or follicular.

K. Endometrial Carcinoma
Authorization of 12 months may be granted for treatment of endometrial carcinoma when either of the following criteria are met:
1. Afinitor is given in combination with letrozole; OR
2. Afinitor is given in combination with letrozole as adjuvant treatment for surgically staged members.

L. Central Nervous System Cancers
1. Authorization of 12 months may be granted for the treatment of glioma (including glioblastoma) or meningioma.
2. Authorization of 12 months may be granted for the adjuvant treatment of subependymal giant cell astrocytoma (SEGA) as a single agent.

III. CONTINUATION OF THERAPY
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES


## STEP THERAPY CRITERIA

<table>
<thead>
<tr>
<th>BRAND NAME*</th>
</tr>
</thead>
<tbody>
<tr>
<td>(generic)</td>
</tr>
<tr>
<td>ALDARA (BRAND ONLY)</td>
</tr>
<tr>
<td>ZYCLARA (BRAND ONLY)</td>
</tr>
</tbody>
</table>

### Status: CVS Caremark Criteria

**Type: Initial Step Therapy with Quantity Limit;**

**Post Step Therapy Prior Authorization with Quantity Limit**   Ref # 1377-E

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

### FDA-APPROVED INDICATIONS

#### Aldara

**Actinic Keratosis**

Aldara Cream is indicated for the topical treatment of clinically typical, nonhyperkeratotic, nonhypertrophic actinic keratoses on the face or scalp in immunocompetent adults.

**Superficial Basal Cell Carcinoma**

Aldara Cream is indicated for the topical treatment of biopsy-confirmed, primary superficial basal cell carcinoma (sBCC) in immunocompetent adults, with a maximum tumor diameter of 2.0 cm, located on the trunk (excluding anogenital skin), neck, or extremities (excluding hands and feet), only when surgical methods are medically less appropriate and patient follow-up can be reasonably assured. The histological diagnosis of superficial basal cell carcinoma should be established prior to treatment, since safety and efficacy of Aldara Cream have not been established for other types of basal cell carcinomas, including nodular and morpheaform (fibrosing or sclerosing) types.

**External Genital Warts**

Aldara Cream is indicated for the treatment of external genital and perianal warts/condyloma acuminata in patients 12 years or older.

**Limitations of Use**

Aldara Cream has been evaluated in children ages 2 to 12 years with molluscum contagiosum and these studies failed to demonstrate efficacy.

**Unevaluated Populations**

The safety and efficacy of Aldara Cream in immunosuppressed patients have not been established. Aldara Cream should be used with caution in patients with pre-existing autoimmune conditions. The efficacy and safety of Aldara Cream have not been established for patients with Basal Cell Nevus Syndrome or Xeroderma Pigmentosum.

#### Zyclara

**Actinic Keratosis**

Zyclara Cream, 2.5% and 3.75% are indicated for the topical treatment of clinically typical, visible or palpable actinic keratoses (AK) of the full face or balding scalp in immunocompetent adults.

**External Genital Warts**

Zyclara Cream, 3.75% is also indicated for the treatment of external genital (EGW) and perianal warts/condyloma acuminata in patients 12 years or older.

### INITIAL STEP THERAPY with QUANTITY LIMIT*

If the patient has filled a prescription for at least a 30 day supply of generic imiquimod 5% cream within the past 120 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.* If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating
that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

*If the patient meets the initial step therapy criteria, then the initial limit criteria will apply. If the patient is requesting more than the initial quantity limit the claim will reject with a message indicating that a PA is required.

**INITIAL QUANTITY LIMIT**

<table>
<thead>
<tr>
<th>Drug</th>
<th>4 Week Limit*</th>
<th>12 Week Limit*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aldara packets</td>
<td>2 boxes (24 packets) / 21 days</td>
<td>6 boxes (72 packets) / 63 days</td>
</tr>
<tr>
<td>Zyclara packets</td>
<td>1 box (28 packets) / 21 days</td>
<td>3 boxes (84 packets) / 63 days</td>
</tr>
<tr>
<td>Zyclara pump</td>
<td>1 pump (7.5gm) / 21 days</td>
<td>3 pumps (7.5gms each) / 63 days</td>
</tr>
</tbody>
</table>

*The duration of 21 days is used for a 28-day fill period and 63 days is used for an 84-day fill period to allow time for refill processing.

**COVERAGE CRITERIA**
The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has experienced an inadequate treatment response, intolerance, or contraindication to generic imiquimod 5 percent cream

**AND**

- The request is for the treatment of superficial basal cell carcinoma with Aldara

**OR**

- The request is for the treatment of actinic keratosis or external genital warts

Quantity Limit applies.

**RATIONALE**
If the patient has filled a prescription for at least a 30 day supply of generic imiquimod 5% cream within the past 120 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. The quantity limit is set at 2 boxes of Aldara or 1 box of Zyclara or 1 pump of Zyclara per month.

If the patient does not meet the initial step therapy criteria, then prior authorization (PA) is required. If the patient is requesting more than the initial quantity limit the claim will reject with a message indicating that a PA is required.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Aldara cream is indicated for actinic keratosis, superficial basal cell carcinoma, and external genital warts. Zyclara cream is indicated for actinic keratosis and external genital and perianal warts in patients 12 years or older.

Imiquimod 5% cream is indicated for the topical treatment of clinically typical, nonhyperkeratotic, nonhypertrophic actinic keratoses on the face or scalp in immunocompetent adults. According to the American Academy of Dermatology, no one treatment works on all actinic keratosis. Clearance rates are dependent on patient adherence and there is limited evidence regarding comparative efficacy of topical medications. Therefore, the patient must have experienced an inadequate treatment response or intolerance to generic imiquimod 5% cream.

For actinic keratosis, Aldara Cream should be applied 2 times per week for a full 16 weeks to a defined treatment area on the face or scalp (but not both concurrently). The treatment area is defined as one contiguous area of approximately 25 cm² (e.g., 5 cm × 5 cm) on the face (e.g., forehead or one cheek) or on the scalp. For superficial basal cell carcinoma, Aldara Cream should be applied 5 times per week for a full 6 weeks to a biopsy-confirmed superficial basal cell carcinoma. For external genital/perianal warts, Aldara Cream should be applied 3 times per week. Aldara Cream treatment should continue until there is total clearance of the genital/perianal warts or for a maximum of 16 weeks. New warts may develop during therapy, as Aldara Cream is not a cure.
Aldara Cream is packaged in single-use packets each of which contains 250 mg of the cream, equivalent to 12.5 mg of imiquimod, with 12 packets supplied per box. Therefore, the quantity limit is set to 2 boxes (24 packets) per 4 weeks which allows a quantity sufficient for all Food and Drug Administration (FDA) approved indications.

For actinic keratosis, Zyclara Cream should be applied once per day before bedtime to the affected treatment area on the face or scalp for two 2-week treatment cycles divided by a 2-week no-treatment period. The treatment area is defined as one contiguous area of approximately 25 cm² (e.g., 5 cm × 5 cm²) on the face (e.g., forehead or one cheek) or on the scalp. Patients may apply up to 0.5 grams or 2 packets or 2 full actuations of the pump to each treatment area and left on the skin for approximately 8 hours. For external genital and perianal warts, Zyclara Cream should be applied once per day until total clearance or for up to 8 weeks. Patients may apply up to 0.25 grams or one packet or one full actuation of the pump to each treatment area and left on the skin for approximately 8 hours. No more than 2 boxes (56 packets) or two 7.5 gram pumps should be prescribed per two 2-week treatment cycles and treatment cycles should not be extended due to missed doses.

Zyclara 3.75% Cream is packaged in single-use packets, with 28 packets supplied per box and a 7.5 gram pump. Each pump, when actuated after priming delivers 0.235 grams of cream. Each 3.75% Cream packet delivers 0.25 grams of cream. Therefore, the quantity limit is set to 1 box (28 packets) and 1 pump (7.5gm) per 4 weeks which allows a quantity sufficient for all Food and Drug Administration (FDA) approved indications.

### Recommended Dosing Chart

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Diagnosis</th>
<th>Dosage</th>
<th>Treatment Course Duration</th>
<th>Quantity per 4 weeks</th>
<th>Quantity per treatment course</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aldara</td>
<td>Superficial basal cell carcinoma</td>
<td>1 packet 5 times per week</td>
<td>6 weeks</td>
<td>20 packets up to 2 boxes</td>
<td>30 packets up to 3 boxes</td>
</tr>
<tr>
<td>Aldara</td>
<td>Actinic Keratosis</td>
<td>1 packet 2 times per week</td>
<td>16 weeks</td>
<td>8 packets up to 1 box</td>
<td>32 packets up to 3 boxes</td>
</tr>
<tr>
<td>Aldara</td>
<td>External genital warts</td>
<td>1 packet 3 times per week</td>
<td>16 weeks</td>
<td>12 packets 1 box</td>
<td>48 packets 4 boxes</td>
</tr>
<tr>
<td>Zyclara 3.75% 28 packets per box</td>
<td>Actinic Keratosis</td>
<td>2 packets per day</td>
<td>two 2-weeks divided by 2-weeks off</td>
<td>28 packets 1 box</td>
<td>56 packets 2 boxes</td>
</tr>
<tr>
<td>Zyclara 3.75% 28 packets per box</td>
<td>External genital warts</td>
<td>1 packet per day</td>
<td>8 weeks</td>
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</tr>
<tr>
<td>Zyclara 28 actuations per 7.5 gram pump</td>
<td>Actinic Keratosis</td>
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</tr>
</tbody>
</table>

**REFERENCES**

CRITERIA FOR APPROVAL

1. Is this request for the treatment of any of the following: A) actinic keratosis, B) external genital warts, C) superficial basal cell carcinoma with Aldara?
   - Yes
   - No

2. Has the patient experienced an inadequate treatment response, intolerance, or contraindication to generic imiquimod 5 percent cream?
   - Yes
   - No

3. Does the patient require MORE than any of the following per month: A) 2 boxes (24 packets) of Aldara, B) 1 box (28 packets) of Zyclara, C) one 7.5 gram pump of Zyclara?
   [RPh Note: If yes, then deny and enter a partial approval for 2 boxes (24 packets) per 21 days of brand Aldara, or 1 box (28 packets) or one 7.5 gram pump per 21 days of brand Zyclara.]
   - Yes
   - No

Mapping Instructions

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
<th>DENIAL REASONS – DO NOT USE FOR MEDICARE PART D</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Go to 2</td>
<td>Deny You do not meet the requirements of your plan. Your plan covers this drug when you have any of the following: - actinic keratosis - external genital warts - superficial basal cell carcinoma (Aldara only). Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]</td>
</tr>
<tr>
<td>2.</td>
<td>Go to 3</td>
<td>Deny You do not meet the requirements of your plan. Your plan covers this drug when you have tried generic imiquimod 5 percent cream and it either did not work for you or you cannot use it. Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance or contraindication to generic imiquimod 5 percent cream]</td>
</tr>
<tr>
<td>3.</td>
<td>Deny</td>
<td>Approve, 12 months, See Quantity Limits Chart* You do not meet the requirements of your plan. You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to one of the following per month: - 2 boxes (24 packets) of brand Aldara - 1 box (28 packets) of brand Zyclara - one 7.5 gram pump of brand Zyclara. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. Your request has been denied based on the information we have. [Short Description: Over max quantity]</td>
</tr>
</tbody>
</table>

* QUANTITY LIMITS CHART
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SPECIALTY GUIDELINE MANAGEMENT

ALDURAZYME (laronidase)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Aldurazyme is indicated for patients with Hurler and Hurler-Scheie forms of Mucopolysaccharidosis I (MPS I) and for patients with the Scheie form who have moderate to severe symptoms. The risks and benefits of treating mildly affected patients with the Scheie form have not been established.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Mucopolysaccharidosis I (MPS I)
Indefinite authorization may be granted for treatment of MPS I when both of the following criteria are met:
A. Diagnosis of MPS I was confirmed by enzyme assay demonstrating a deficiency of alpha-L-iduronidase enzyme activity or by genetic testing.
B. Member has the Hurler or Hurler-Scheie form of MPS I OR the member has the Scheie form (Scheie syndrome) with moderate to severe symptoms.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

ALECENSA (alectinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Alecensa is indicated for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive, metastatic non-small cell lung cancer (NSCLC) as detected by an FDA-approved test.

B. Compendial Uses

1. Recurrent or advanced NSCLC, ALK rearrangement-positive
2. Brain metastases from ALK rearrangement-positive NSCLC

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: ALK mutation status

III. CRITERIA FOR INITIAL APPROVAL

Non-Small Cell Lung Cancer (NSCLC)
Authorization of 12 months may be granted for treatment of recurrent, advanced or metastatic ALK-positive NSCLC (including brain metastases from NSCLC).

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced an unacceptable toxicity.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

ALIMTA (pemetrexed)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Nonsquamous non-small cell lung cancer (NSCLC)
   a. Alimta is indicated in combination with cisplatin therapy for the initial treatment of patients with locally advanced or metastatic nonsquamous NSCLC.
   b. Alimta is indicated for the maintenance treatment of patients with locally advanced or metastatic nonsquamous NSCLC whose disease has not progressed after four cycles of platinum-based first-line chemotherapy.
   c. Alimta is indicated as a single agent for the treatment of patients with locally advanced or metastatic nonsquamous NSCLC after prior chemotherapy.

   Limitations of use: Alimta is not indicated for the treatment of patients with squamous cell NSCLC.

2. Malignant pleural mesothelioma (MPM)
   Alimta in combination with cisplatin is indicated for the treatment of patients with MPM whose disease is unresectable or who are otherwise not candidates for curative surgery.

B. Compendial Uses

1. Bladder cancer, primary carcinoma of the urethra, upper genitourinary (GU) tract tumors, and urothelial carcinoma of the prostate
2. Malignant pleural mesothelioma
3. Nonsquamous NSCLC
4. Ovarian cancer (epithelial histology), fallopian tube cancer, and primary peritoneal cancer
5. Primary central nervous system (CNS) lymphoma
6. Thymoma and thymic carcinoma
7. Malignant peritoneal mesothelioma

All other indications are considered experimental/investigational and are not a covered benefit.

II. EXCLUSIONS

Coverage will not be provided for members with any of the following exclusions: Squamous cell NSCLC

III. CRITERIA FOR INITIAL APPROVAL

A. Bladder Cancer, Primary Carcinoma of the Urethra, Upper Genitourinary Tract Tumors, or Urothelial Carcinoma of the Prostate
1. **Bladder Cancer**
   Authorization of 12 months may be granted for treatment of bladder cancer.

2. **Primary Carcinoma of the Urethra, Upper Genitourinary Tract Tumors, or Urothelial Carcinoma of the Prostate**
   Authorization of 12 months may be granted for treatment of recurrent or metastatic primary carcinoma of the urethra, upper genitourinary tract tumors, or urothelial carcinoma of the prostate.

B. **Malignant Pleural Mesothelioma (MPM)**
   Authorization of 12 months may be granted for treatment of MPM.

C. **Non-Small Cell Lung Cancer (Non-Squamous)**
   Authorization of 12 months may be granted for treatment of non-squamous non-small cell lung cancer.

D. **Ovarian Cancer (Epithelial)/Fallopian Tube Cancer/Primary Peritoneal Cancer**
   Authorization of 12 months may be granted for treatment of persistent or recurrent epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer.

E. **Primary CNS Lymphoma**
   Authorization of 12 months may be granted for treatment of relapsed or refractory primary CNS lymphoma.

F. **Thymoma and Thymic Carcinoma**
   Authorization of 12 months may be granted for treatment of thymoma or thymic carcinoma.

G. **Malignant Peritoneal Mesothelioma (MPeM)**
   Authorization of 12 months may be granted for treatment of MPeM.

IV. **CONTINUATION OF THERAPY**

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. **DOSAGE AND ADMINISTRATION**

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

VI. **REFERENCES**

SPECIALTY GUIDELINE MANAGEMENT

ALIQOPA (copanlisib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   Aliqopa is indicated for the treatment of adult patients with relapsed follicular lymphoma (FL) who have received at least two prior systemic therapies.

   Accelerated approval was granted for this indication based on overall response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

B. Compendial Uses
   Refractory (to at least two prior therapies) or progressive follicular lymphoma

   All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Follicular lymphoma
Authorization of 12 months may be granted for treatment of follicular lymphoma (FL) when EITHER of the following criteria is met:
1. The member has progressive FL, OR
2. The member has relapsed or refractory FL and has received at least two prior therapies.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT
Alpha₁-Proteinase Inhibitors

ARALAST NP (alpha₁-proteinase inhibitor [human])
GLASSIA (alpha₁-proteinase inhibitor [human])
PROLASTIN-C (alpha₁-proteinase inhibitor [human])
ZEMAIRA (alpha₁-proteinase inhibitor [human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
1. Aralast NP
   Chronic augmentation therapy in adults with clinically evident emphysema due to severe congenital deficiency of alpha₁-proteinase inhibitor (alpha₁-antitrypsin deficiency)

2. Glassia
   Chronic augmentation and maintenance therapy in adults with clinically evident emphysema due to severe hereditary deficiency of alpha₁-proteinase inhibitor (alpha₁-antitrypsin deficiency)

3. Prolastin-C
   Chronic augmentation and maintenance therapy in adults with clinical evidence of emphysema due to severe hereditary deficiency of alpha₁-proteinase inhibitor (alpha₁-antitrypsin deficiency)

4. Zemaira
   Chronic augmentation and maintenance therapy in adults with alpha₁-proteinase inhibitor deficiency and clinical evidence of emphysema

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Indefinite authorization may be granted for treatment of alpha₁-antitrypsin (AAT) deficiency when all of the following criteria are met:
1. The member has clinically evident emphysema.
2. The member’s pretreatment serum AAT level is less than 11 micromol/L (80 mg/dL by radial immunodiffusion or 50 mg/dL by nephelometry).
3. The member’s pretreatment post-bronchodilation forced expiratory volume in 1 second (FEV₁) is greater than or equal to 25% and less than or equal to 80% of the predicted value.
III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

ALUNBRIG (brigatinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Alunbrig is indicated for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) who have progressed on or are intolerant to crizotinib.

This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

B. Compendial Uses

1. Recurrent, advanced or metastatic ALK rearrangement-positive NSCLC: as first line therapy, after progression on or intolerance to crizotinib, or as continuation of therapy if used first line
2. Brain metastases from ALK rearrangement-positive NSCLC

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: ALK mutation status

III. CRITERIA FOR INITIAL APPROVAL

Non-Small Cell Lung Cancer (NSCLC)

Authorization of 12 months may be granted for treatment of recurrent, advanced or metastatic ALK-positive NSCLC (including brain metastases from NSCLC).

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced an unacceptable toxicity.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

Letairis (ambrisentan)
ambrisentan

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
A. To improve exercise ability and delay clinical worsening
B. In combination with tadalafil to reduce the risks of disease progression and hospitalization for worsening PAH, and to improve exercise ability.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Pulmonary Arterial Hypertension (PAH)
Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:
A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
B. PAH was confirmed by either criterion (1) or criterion (2) below:
   1. Pretreatment right heart catheterization with all of the following results:
      i. mPAP ≥ 25 mmHg
      ii. PCWP ≤ 15 mmHg
      iii. PVR > 3 Wood units
   2. For infants less than one year of age with any of the following conditions, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed:
      i. Post cardiac surgery
      ii. Chronic heart disease
      iii. Chronic lung disease associated with prematurity
      iv. Congenital diaphragmatic hernia

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section II who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. APPENDIX

ambrisentan-Letairis 1646-A SGM P2019 © 2019 CVS Caremark. All rights reserved.

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WHO Classification of Pulmonary Hypertension

1 PAH
1.1 Idiopathic (PAH)
1.2 Heritable PAH
1.3 Drug- and toxin-induced PAH
1.4. PAH associated with:
   1.4.1 Connective tissue diseases
   1.4.2 HIV infection
   1.4.3 Portal hypertension
   1.4.4 Congenital heart diseases
   1.4.5 Schistosomiasis
1.5 PAH long-term responders to calcium channel blockers
1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease
2.1 PH due to heart failure with preserved LVEF
2.2 PH due to heart failure with reduced LVEF
2.3 Valvular heart disease
2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia
3.1 Obstructive lung disease
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction
4.1 Chronic thromboembolic PH
4.2 Other pulmonary artery obstructions
   4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
   4.2.2 Other malignant tumors
      Renal carcinoma
      Uterine carcinoma
      Germ cell tumours of the testis
      Other tumours
   4.2.3 Non-malignant tumours
      Uterine leiomyoma
   4.2.4 Arteritis without connective tissue disease
   4.2.5 Congenital pulmonary artery stenosis
   4.2.6 Parasites
      Hydatidosis

5 PH with unclear and/or multifactorial mechanisms
5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
5.4 Complex congenital heart disease

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

AMPYRA (dalfampridine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication: Ampyra is indicated as a treatment to improve walking in adult patients with multiple sclerosis. This was demonstrated by an increase in walking speed.

All other indications are considered experimental/investigational and are not covered benefits.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 30 days may be granted to members with a diagnosis of multiple sclerosis if the member has sustained walking impairment (prior to initiating therapy with Ampyra).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted to members with multiple sclerosis if the member has experienced an improvement in walking speed or other objective measure of walking ability since starting Ampyra.

IV. REFERENCES

# PRIOR AUTHORIZATION CRITERIA

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<tr>
<th>DRUG CLASS</th>
<th>TOPICAL ANTIFUNGAL AGENTS (BRAND PRODUCTS ONLY)</th>
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<td>(miconazole/zinc oxide/white petrolatum)</td>
</tr>
<tr>
<td>XOLEGEL</td>
<td>(ketoconazole)</td>
</tr>
</tbody>
</table>

*Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*
FDA-APPROVED INDICATIONS

Ecoza
Ecoza topical 1% foam is indicated for the treatment of interdigital tinea pedis caused by *Trichophyton rubrum*, *Trichophyton mentagrophytes*, and *Epidermophyton floccosum* in patients 12 years of age and older.

Ertaczo
Ertaczo 2% cream is indicated for the topical treatment of interdigital tinea pedis in immunocompetent patients 12 years of age and older, caused by: *Trichophyton rubrum*, *Trichophyton mentagrophytes*, and *Epidermophyton floccosum*.

Exelderm
Exelderm 1% cream is indicated for the treatment of tinea pedis (athlete's foot), tinea cruris, and tinea corporis caused by *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Epidermophyton floccosum*, and *Microsporum canis*, and for the treatment of tinea versicolor.

Exelderm 1% solution is indicated for the treatment of tinea cruris and tinea corporis caused by *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Epidermophyton floccosum*, and *Microsporum canis*; and for the treatment of tinea versicolor.

Effectiveness has not been proven in tinea pedis (athlete’s foot). Symptomatic relief usually occurs within a few days after starting Exelderm solution and clinical improvement usually occurs within one week.

Loprox
Loprox 1% shampoo is indicated for the topical treatment of seborrheic dermatitis of the scalp in adults.

Lotrisone
Lotrisone cream is a combination of an azole antifungal and corticosteroid and is indicated for the topical treatment of symptomatic inflammatory tinea pedis, tinea cruris, and tinea corporis due to *Epidermophyton Floccosum*, *Trichophyton Mentagrophytes*, and *Trichophyton rubrum* in patients 17 years and older.

Luzu
Luzu cream is indicated for the topical treatment of interdigital tinea pedis, tinea cruris, and tinea corporis caused by the organisms *Trichophyton rubrum* and *Epidermophyton floccosum*.

Mentax
Mentax 1% cream is indicated for the topical treatment of the dermatologic infection, tinea (pityriasis) versicolor due to *M. furfur* (formerly *P. orbiculare*). Butenafine HCl cream was not studied in immunocompromised patients.

Naftin
Naftin 1% gel is indicated for the topical treatment of tinea pedis, tinea cruris, and tinea corporis caused by the organisms *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Trichophyton tonsurans*, *Epidermophyton floccosum*.

Naftin 2% cream is an allylamine antifungal indicated for the treatment of interdigital tinea pedis, tinea cruris, and tinea corporis caused by the organism *Trichophyton rubrum*.

Naftin 2% gel is an allylamine antifungal indicated for the treatment of interdigital tinea pedis caused by the organisms *Trichophyton rubrum*, *Trichophyton mentagrophytes*, and *Epidermophyton floccosum*.

Oxistat
Oxistat 1% lotion is indicated for the topical treatment of the following dermal infections: tinea pedis, tinea cruris, and tinea corporis due to *Trichophyton rubrum*, *Trichophyton mentagrophytes*, or *Epidermophyton floccosum*.

Oxistat 1% cream is indicated for the topical treatment of the following dermal infections: tinea pedis, tinea cruris, and tinea corporis due to *Trichophyton rubrum*, *Trichophyton mentagrophytes*, or *Epidermophyton floccosum*. Oxistat 1% cream is also indicated for the topical treatment of tinea (pityriasis) versicolor due to *Malassezia furfur*.
Vusion
Vusion ointment is indicated for the adjunctive treatment of diaper dermatitis only when complicated by documented candidiasis (microscopic evidence of pseudohyphae and/or budding yeast), in immunocompetent pediatric patients 4 weeks and older. A positive fungal culture for *Candida albicans* is not adequate evidence of candidal infection since colonization with *C. albicans* can result in a positive culture. The presence of candidal infection should be established by microscopic evaluation prior to initiating treatment.

Vusion should be used as part of a treatment regimen that includes measures directed at the underlying diaper dermatitis, including gentle cleansing of the diaper area and frequent diaper changes.

Vusion should not be used as a substitute for frequent diaper changes. Vusion should not be used to prevent the occurrence of diaper dermatitis, since preventative use may result in the development of drug resistance.

Limitations of Use
The safety and efficacy of Vusion have not been demonstrated in immunocompromised patients, or in infants less than 4 weeks of age (premature or term).

The safety and efficacy of Vusion have not been evaluated in incontinent adult patients. Vusion should not be used to prevent the occurrence of diaper dermatitis, such as in an adult institutional setting, since preventative use may result in the development of drug resistance.

Xolegel
Xolegel is indicated for the topical treatment of seborrheic dermatitis in immunocompetent adults and children 12 years of age and older.

Safety and efficacy of Xolegel for treatment of fungal infections have not been established.

**COVERAGE CRITERIA**
The requested drug will be covered with prior authorization when the following criteria are met:
- The requested drug is being used for an FDA-Approved indication

**RATIONALE**
The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Ecoza topical 1% foam is indicated for the treatment of interdigital tinea pedis in patients 12 years of age and older. Ertaczo 2% cream is indicated for the topical treatment of interdigital tinea pedis in immunocompetent patients 12 years of age and older. Exelderm 1% cream is indicated for the treatment of tinea pedis (athlete’s foot), tinea cruris, and tinea corporis and for the treatment of tinea versicolor. Exelderm 1% solution is indicated for the treatment of tinea cruris and tinea corporis and for the treatment of tinea versicolor. Loprox 1% shampoo is indicated for the topical treatment of seborrheic dermatitis of the scalp in adults. Lotrison cream is indicated for the topical treatment of symptomatic inflammatory tinea pedis, tinea cruris, and tinea corporis. Luzu cream is indicated for the topical treatment of interdigital tinea pedis, tinea cruris, and tinea corporis. Mentax 1% cream is indicated for the topical treatment of the dermatologic infection, tinea ( pityriasis) versicolor. Butenafine HCl cream was not studied in immunocompromised patients. Naftin 1% gel is indicated for the topical treatment of tinea pedis, tinea cruris, and tinea corporis. Naftin 2% gel is indicated for the treatment of interdigital tinea pedis. Oxistat 1% cream and lotion are indicated for the topical treatment of tinea pedis, tinea cruris, and tinea corporis. Oxistat 1% cream is also indicated for the topical treatment of tinea ( pityriasis) versicolor. Vusion ointment is indicated for the adjunctive treatment of diaper dermatitis only when complicated by documented candidiasis (microscopic evidence of pseudohyphae and/or budding yeast), in immunocompetent pediatric patients 4 weeks and older. Xolegel is indicated for the topical treatment of seborrheic dermatitis in immunocompetent adults and children 12 years of age and older.
REFERENCES


Written by: UM Development (MS)
Date Written: 06/2016
Revised: (CT) 08/2016 (added target drugs); (SF) 06/2017 (no clinical changes); (DS) 06/2018 (no clinical changes), 06/2019 (no clinical changes)
Reviewed: Medical Affairs (MM) 06/2016
External Review: 09/2016, 10/2017, 10/2018, 10/2019

CRITERIA FOR APPROVAL

| 1. Is the requested drug being used for an FDA-Approved indication? | Yes | No |

Guidelines for Approval

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DENIAL REASONS – DO NOT USE FOR MEDICARE PART D

1. Approve, 3 months
   Deny
   You do not meet the requirements of your plan. Your plan covers the requested drug when it is used for the FDA-approved use. Your request has been denied based on the information we have.
   [Short Description: No approvable diagnosis]
## STEP THERAPY CRITERIA

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**Status:** CVS Caremark Criteria  
**Type:** Initial Step Therapy; Post Step Therapy Prior Authorization  
**Ref # 1380-D**

*Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*
**FDA-APPROVED INDICATIONS**

**Ecoza**
Ecoza topical 1% foam is indicated for the treatment of interdigital tinea pedis caused by *Trichophyton rubrum*, *Trichophyton mentagrophytes*, and *Epidermophyton floccosum* in patients 12 years of age and older.

**Ertaczo**
Ertaczo 2% cream is indicated for the topical treatment of interdigital tinea pedis in immunocompetent patients 12 years of age and older, caused by *Trichophyton rubrum*, *Trichophyton mentagrophytes*, and *Epidermophyton floccosum*.

**Exelderm**
Exelderm 1% cream is indicated for the treatment of tinea pedis (athlete’s foot), tinea cruris, and tinea corporis caused by *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Epidermophyton floccosum*, and *Microsporum canis*, and for the treatment of tinea versicolor.

Exelderm 1% solution is indicated for the treatment of tinea cruris and tinea corporis caused by *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Epidermophyton floccosum*, and *Microsporum canis*; and for the treatment of tinea versicolor.

Effectiveness has not been proven in tinea pedis (athlete’s foot). Symptomatic relief usually occurs within a few days after starting Exelderm solution and clinical improvement usually occurs within one week.

**Loprox**
Loprox 1% shampoo is indicated for the topical treatment of seborrheic dermatitis of the scalp in adults.

**Lotrisone**
Lotrisone cream is a combination of an azole antifungal and corticosteroid and is indicated for the topical treatment of symptomatic inflammatory tinea pedis, tinea cruris, and tinea corporis due to *Epidermophyton Floccosum*, *Trichophyton Mentagrophytes*, and *Trichophyton rubrum* in patients 17 years and older.

**Luzu**
Luzu cream is indicated for the topical treatment of interdigital tinea pedis, tinea cruris, and tinea corporis caused by the organisms *Trichophyton rubrum* and *Epidermophyton floccosum*.

**Mentax**
Mentax 1% cream is indicated for the topical treatment of the dermatologic infection, tinea (pityriasis) versicolor due to *M. furfur* (formerly *P. orbiculare*). Butenafine HCl cream was not studied in immunocompromised patients.

**Naftin**
Naftin 1% gel is indicated for the topical treatment of tinea pedis, tinea cruris, and tinea corporis caused by the organisms *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Trichophyton tonsurans*, *Epidermophyton floccosum*.

Naftin 2% cream is an allylamine antifungal indicated for the treatment of interdigital tinea pedis, tinea cruris, and tinea corporis caused by the organism *Trichophyton rubrum*.

Naftin 2% gel is an allylamine antifungal indicated for the treatment of interdigital tinea pedis caused by the organisms *Trichophyton rubrum*, *Trichophyton mentagrophytes*, and *Epidermophyton floccosum*.

**Oxistat**
Oxistat 1% lotion is indicated for the topical treatment of the following dermal infections: tinea pedis, tinea cruris, and tinea corporis due to *Trichophyton rubrum*, *Trichophyton mentagrophytes*, or *Epidermophyton floccosum*.

Oxistat 1% cream is indicated for the topical treatment of the following dermal infections: tinea pedis, tinea cruris, and tinea corporis due to *Trichophyton rubrum*, *Trichophyton mentagrophytes*, or *Epidermophyton floccosum*. Oxistat 1% cream is also indicated for the topical treatment of tinea (pityriasis) versicolor due to *Malassezia furfur*.
Vusion
Vusion ointment is indicated for the adjunctive treatment of diaper dermatitis only when complicated by documented candidiasis (microscopic evidence of pseudohyphae and/or budding yeast), in immunocompetent pediatric patients 4 weeks and older. A positive fungal culture for Candida albicans is not adequate evidence of candidal infection since colonization with C. albicans can result in a positive culture. The presence of candidal infection should be established by microscopic evaluation prior to initiating treatment.

Vusion should be used as part of a treatment regimen that includes measures directed at the underlying diaper dermatitis, including gentle cleansing of the diaper area and frequent diaper changes.

Vusion should not be used as a substitute for frequent diaper changes. Vusion should not be used to prevent the occurrence of diaper dermatitis, since preventative use may result in the development of drug resistance.

Limitations of Use
The safety and efficacy of Vusion have not been demonstrated in immunocompromised patients, or in infants less than 4 weeks of age (premature or term).

The safety and efficacy of Vusion have not been evaluated in incontinent adult patients. Vusion should not be used to prevent the occurrence of diaper dermatitis, such as in an adult institutional setting, since preventative use may result in the development of drug resistance.

Xolegel
Xolegel is indicated for the topical treatment of seborrheic dermatitis in immunocompetent adults and children 12 years of age and older.

Safety and efficacy of Xolegel for treatment of fungal infections have not been established.

INITIAL STEP THERAPY
If the patient has filled a prescription for at least a 7 day supply of a generic topical antifungal agent within the past 120 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:
- The patient experienced an inadequate treatment response, intolerance, or contraindication to a generic topical antifungal agent (e.g., ciclopirox, clotrimazole, ketoconazole, naftifine, oxiconazole)

RATIONALE
If the patient has filled a prescription for at least a 7 day supply of a generic topical antifungal agent within the past 120 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

If the patient does not meet the initial step therapy criteria, then prior authorization is required.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines.

Ecoza topical 1% foam is indicated for the treatment of interdigital tinea pedis in patients 12 years of age and older.
Ertaczo 2% cream is indicated for the topical treatment of interdigital tinea pedis in immunocompetent patients 12 years of age and older.
Exelderm 1% cream is indicated for the treatment of tinea pedis (athlete’s foot), tinea cruris, and tinea corporis and for the treatment of tinea versicolor.
Exelderm 1% solution is indicated for the treatment of tinea cruris and
tinea corporis and for the treatment of tinea versicolor. Loprox 1% shampoo is indicated for the topical treatment of seborrheic dermatitis of the scalp in adults. Lotrisone cream is indicated for the topical treatment of symptomatic inflammatory tinea pedis, tinea cruris, and tinea corporis. Luzu cream is indicated for the topical treatment of interdigital tinea pedis, tinea cruris, and tinea corporis. Mentax 1% cream is indicated for the topical treatment of the dermatologic infection, tinea (pityriasis) versicolor. Butenafine HCl cream was not studied in immunocompromised patients. Naftin 1% gel is indicated for the topical treatment of tinea pedis, tinea cruris, and tinea corporis. Naftin 2% cream is indicated for the treatment of interdigital tinea pedis, tinea cruris, and tinea corporis. Naftin 2% gel is indicated for the treatment of interdigital tinea pedis. Oxistat 1% cream and lotion are indicated for the topical treatment of tinea pedis, tinea cruris, and tinea corporis. Oxistat 1% cream is also indicated for the topical treatment of tinea (pityriasis) versicolor. Vusion ointment is indicated for the adjunctive treatment of diaper dermatitis only when complicated by documented candidiasis (microscopic evidence of pseudohyphae and/or budding yeast), in immunocompetent pediatric patients 4 weeks and older. Xolegel is indicated for the topical treatment of seborrheic dermatitis in immunocompetent adults and children 12 years of age and older.

Treatment for seborrheic dermatitis includes over-the-counter shampoos and topical antifungals, calcineurin inhibitors, and corticosteroids. For long-term control, antifungal shampoos containing ketoconazole 2% or ciclopirox 1% (Loprox) can be used daily or at least two or three times per week for several weeks. If a patient with seborrheic dermatitis shows no clinical improvement after 4 weeks of treatment, the diagnosis should be reviewed.

Tinea corporis and tinea cruris generally can be effectively treated using a topical antifungal. Many clinicians consider topical imidazole derivative azole antifungals (e.g., clotrimazole, ketoconazole, oxiconazole) or topical allylamine antifungals (e.g., naftin) the drugs of first choice for the topical treatment of tinea corporis or tinea cruris, although other antifungals agents (e.g., ciclopirox ointment) also can be effective in the treatment of these infections. Uncomplicated interdigital and vesiculobullous forms of tinea pedis generally can be treated effectively using topical therapy with an imidazole derivative azole antifungal (e.g., clotrimazole, ketoconazole, oxiconazole), an allylamine antifungal (e.g., naftin), or other topical antifungal agents such as ciclopirox olamine. Like other imidazole derivatives (e.g., clotrimazole, ketoconazole) and ciclopirox ointment, oxiconazole has an advantage over some other topical antifungal agents (e.g., nystatin, tolnaftate) in the treatment of mixed infections or for empiric treatment pending identification of the causative organism, since the drug is active against both dermatophytes and Candida. If clinical improvement does not occur after 4 weeks of treatment with topical treatment, the diagnosis should be reevaluated.

Pityriasis (tinea) versicolor generally can be treated topically with an imidazole derivative azole antifungal (e.g., clotrimazole, ketoconazole, oxiconazole), ciclopirox olamine. Pityriasis (tinea) versicolor should be treated for 2 weeks to reduce the possibility of recurrence. If clinical improvement does not occur after the recommended treatment period, the diagnosis should be reevaluated.

The management of diaper dermatitis includes numerous approaches. Eliminating the causes of diaper dermatitis and using barrier creams may be enough to cure mild cases; however, for the best therapeutic approach, fungal and bacterial investigation should be undertaken when suspected. As candidal infection is quite common in more severe cases of diaper dermatitis, antifungal agents such as clotrimazole, ketoconazole, miconazole, econazole, tioconazole, and ciclopirox can be applied to the diaper area with every diaper change. There is a wide variety of disorders to consider in an infant presenting with an inflamed eruption in the diaper area, and it becomes particularly important to consider other diagnoses when diaper dermatitis fails to respond to therapy.

REFERENCES

Written by: UM Development (CT)
Date Written: 06/2016
Revised: 08/2016 (added target drugs); (SF) 06/2017 (no clinical changes) ; (DS) 06/2018 (no clinical changes) , 06/2019 (no clinical changes)
Reviewed: Medical Affairs (GAD) 06/2016
External Review: 09/2016, 10/2017, 10/2018, 10/2019

CRITERIA FOR APPROVAL

1. Has the patient experienced an inadequate treatment response, intolerance, or contraindication to a generic topical antifungal agent (e.g., ciclopirox, clotrimazole, ketoconazole, naftifine, oxiconazole)?

<table>
<thead>
<tr>
<th>Yes</th>
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<tbody>
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<td>1.</td>
<td>Approve, 3 months</td>
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</table>

DENIAL REASONS – DO NOT USE FOR MEDICARE PART D

You do not meet the requirements of your plan. Your plan covers this drug when you have tried a generic topical antifungal agent (e.g., ciclopirox, clotrimazole, ketoconazole, naftifine, oxiconazole) and it either did not work for you or you cannot use it. Your request has been denied based on the information we have.

[Short Description: No inadequate response, intolerance or contraindication to generic topical antifungals]
# PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>ANTIOBESITY AGENTS</th>
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<tbody>
<tr>
<td>BRAND NAME*</td>
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<tr>
<td></td>
<td>benzphetamine products</td>
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<tr>
<td></td>
<td>diethylpropion products</td>
</tr>
<tr>
<td></td>
<td>phendimetrazine products</td>
</tr>
<tr>
<td></td>
<td>phentermine products</td>
</tr>
</tbody>
</table>

**Status: CVS Caremark Criteria**  
**Type: Initial Prior Authorization**  
Ref # 18-A

*Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

## FDA-APPROVED INDICATIONS

### Benzphetamine

Benzphetamine is indicated in the management of exogenous obesity as a short term (a few weeks) adjunct in a regimen of weight reduction based on caloric restriction in patients with an initial body mass index (BMI) of 30 kg/m² or higher who have not responded to appropriate weight reducing regimen (diet and/or exercise) alone. The limited usefulness of agents of this class should be weighed against possible risks inherent in their use. Benzphetamine is indicated for use as monotherapy only.

**Limitations of Use:**
- The effect on cardiovascular morbidity and mortality has not been established.
- The safety and effectiveness of these agents in combination with other products intended for weight loss, including prescription drugs, over-the-counter drugs, and herbal preparations, have not been established.

### Diethylpropion

Diethylpropion is indicated in the management of exogenous obesity as a short-term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction in patients with an initial body mass index of 30 kg/m² or higher and who have not responded to an appropriate weight reducing regimen (diet and/or exercise) alone. The usefulness of agents of this class should be measured against possible risk factors inherent in their use. Diethylpropion is indicated for use as monotherapy only.

**Limitations of Use:**
- The effect on cardiovascular morbidity and mortality has not been established.
- The safety and effectiveness of these agents in combination with other products intended for weight loss, including prescription drugs, over-the-counter drugs, and herbal preparations, have not been established.

### Phendimetrazine

Phendimetrazine tartrate extended-release capsules are indicated in the management of exogenous obesity as a short term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction in patients with an initial body mass index (BMI) of greater than or equal to 30 kg/m² or greater than or equal to 27 kg/m² in the presence of other risk factors (e.g., controlled hypertension, diabetes, hyperlipidemia) who have not responded to appropriate weight reducing regimen (diet and/or exercise) alone. The limited usefulness of agents of this class should be weighed against possible risks inherent in their use. Phendimetrazine tartrate is indicated for use as monotherapy only.

Phendimetrazine tartrate is indicated in the management of exogenous obesity as a short term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction in patients with an initial body mass index (BMI) of 30 kg/m² or...
higher who have not responded to appropriate weight reducing regimen (diet and/or exercise) alone. The limited usefulness of agents of this class should be weighed against possible risks inherent in their use. Phendimetrazine tartrate is indicated for use as monotherapy only.

Limitations of Use:
- The effect on cardiovascular morbidity and mortality has not been established.
- The safety and effectiveness of these agents in combination with other products intended for weight loss, including prescription drugs, over-the-counter drugs, and herbal preparations, have not been established.

**Phentermine**
Phentermine is indicated as a short-term (a few weeks) adjunct in a regimen of weight reduction based on exercise, behavioral modification, and caloric restriction, in the management of exogenous obesity for patients with an initial body mass index greater than or equal to 30 kg/m², or greater than or equal to 27 kg/m² in the presence of other risk factors (e.g., controlled hypertension, diabetes, hyperlipidemia). The limited usefulness of agents of this class should be measured against possible risk factors inherent in their use.

Limitations of Use:
- The effect on cardiovascular morbidity and mortality has not been established.
- The safety and effectiveness of these agents in combination with other products intended for weight loss, including prescription drugs, over-the-counter drugs, and herbal preparations, have not been established.

**COVERAGE CRITERIA**
The requested drug will be covered with prior authorization when the following criteria are met:
- The patient has not received 3 months of therapy with the requested drug within the past 365 days AND
- The requested drug will be used with a reduced calorie diet and increased physical activity AND
  - The patient has a body mass index (BMI) greater than or equal to 30 kg per square meter OR
  - The patient has a body mass index (BMI) greater than or equal to 27 kg per square meter AND has additional risk factors

**RATIONALE**
The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Anoretics are indicated as a short-term (a few weeks) adjunct to a reduced-calorie diet and increased physical activity, in the management of exogenous obesity for patients with an initial body mass index greater than or equal to 30 kg/m² or greater than or equal to 27 kg/m² in the presence of other risk factors (e.g., controlled hypertension, diabetes, hyperlipidemia).1-7 The limited usefulness of agents of this class should be measured against possible risk factors inherent in their use.

The guidelines state that the purpose of weight loss and weight maintenance is to reduce health risk.8,9 Weight loss programs should begin with a basic regimen consisting of a reduced-calorie diet and increased physical activity. The major role of medications is to help with patient compliance to a weight loss plan. Therefore, drugs should be used as part of a comprehensive weight loss program and should never be used without concomitant lifestyle modification. Drugs may be used as an adjunct to diet and physical activity for patients with a BMI that is greater than or equal to 30 kg/m² or greater than or equal to 27 kg/m² if other risk factors are present (e.g., hypertension, diabetes, dyslipidemia, sleep apnea, cardiovascular disease).8,9

Sympathomimetic amine anorectic drugs have a narrow FDA labeling which reflects on the importance of prevention of inappropriate usage. The FDA approved indication for these agents is for short term treatment only. The safety of long-term anorexiant therapy has not been established conclusively beyond 12 weeks of administration. Therefore, coverage will be limited to a total of 3 months per year of each of the following: benzphetamine, diethylpropion, phendimetrazine or phentermine.

**REFERENCES**
CRITERIA FOR APPROVAL

1. Has the patient received 3 months of therapy with the requested drug within the past 365 days?  
   [Tech note: Verify PA History AND the Prescription History before approving. If the request has been approved for the requested drug in the last 365 days or the patient received a paid claim for the requested drug, forward to RPH for review even if the pop up box asked you to approve it]
   - Yes  
   - No

2. Does the patient have a body mass index (BMI) greater than or equal to 30 kg per square meter?  
   [If yes, then skip to question 4.]
   - Yes  
   - No

3. Does the patient have a body mass index (BMI) greater than or equal to 27 kg per square meter AND has additional risk factors?  
   - Yes  
   - No

4. Will the requested medication be used with a reduced calorie diet and increased physical activity?  
   - Yes  
   - No

Guidelines for Approval

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<th>Duration of Approval</th>
<th>3 Months (90 days of therapy) per year</th>
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Mapping Instructions

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<tbody>
<tr>
<td>Deny</td>
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</table>

You do not meet the requirements of your plan.
<table>
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<tr>
<th>2</th>
<th>Go to 4</th>
<th>Go to 3</th>
</tr>
</thead>
<tbody>
<tr>
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<td>Deny</td>
</tr>
<tr>
<td>4</td>
<td>Approve, 3 months (90 days of therapy) per year.</td>
<td>Deny</td>
</tr>
</tbody>
</table>

Your plan covers this drug when you have not received 3 months of therapy with the requested drug within the past year. 
Your request has been denied based on the information we have.  
[Short Description: Over max plan limit]

You do not meet the requirements of your plan. 
Your plan covers this drug when you meet one of these conditions:  
- You have a body mass index (BMI) of 30 kg per square meter or more  
- You have a body mass index (BMI) of 27 kg per square meter or more  
and you have risk factors  
Your request has been denied based on the information we have.  
[Short Description: Not at BMI requirement]

You do not meet the requirements of your plan. 
Your plan covers this drug when you will diet and exercise while taking this drug. 
Your request has been denied based on the information we have.  
[Short Description: Diet and exercise requirement not met]
SPECIALTY GUIDELINE MANAGEMENT

APOKYN (apomorphine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Acute, intermittent treatment of hypomobility, "off" episodes ("end-of-dose wearing off" and unpredictable "on/off" episodes) in patients with advanced Parkinson’s disease.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR APPROVAL

Authorization of 12 months may be granted for the treatment of acute, intermittent treatment of hypomobility, "off" episodes ("end-of-dose wearing off" and unpredictable "on/off" episodes) for members with advanced Parkinson’s disease.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

ARANESP (darbepoetin alfa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Treatment of anemia due to chronic kidney disease (CKD), including patients on dialysis and patients not on dialysis.
   2. Treatment of anemia in patients with non-myeloid malignancies where anemia is due to the effect of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy.

B. Compendial Uses
   1. Symptomatic anemia in patients with myelodysplastic syndromes (MDS)
   2. Anemia in patients whose religious beliefs forbid blood transfusions
   3. Symptomatic anemia in patients with primary myelofibrosis, post-polycythemia vera myelofibrosis, and post-essential thrombocythemia myelofibrosis
   4. Cancer patients who are undergoing palliative treatment

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Note: Requirements regarding pretreatment hemoglobin level exclude values due to a recent transfusion. All members must be assessed for iron deficiency anemia and have adequate iron stores or are receiving iron therapy before starting Aranesp. Members may not use Aranesp concomitantly with other erythropoiesis stimulating agents.

A. Anemia Due to CKD
   Authorization of 12 weeks may be granted for members with pretreatment hemoglobin < 10 g/dL.

B. Anemia Due to Myelosuppressive Chemotherapy
   Authorization of 12 weeks may be granted for members with nonmyeloid malignancy with pretreatment hemoglobin < 10 g/dL.

C. Anemia in MDS
   Authorization of 12 weeks may be granted for members with pretreatment hemoglobin < 10 g/dL whose pretreatment serum EPO level is < 500 MU/ml.

D. Anemia in Members Whose Religious Beliefs Forbid Blood Transfusions
   Authorization of 12 weeks may be granted for members with pretreatment hemoglobin < 10 g/dL.
E. **Anemia in Primary Myelofibrosis (MF), Post-polycythemia Vera MF, and Post-Essential Thrombocythemia MF**  
Authorization of 12 weeks may be granted for members who meet ALL of the following criteria:  
1. Pretreatment hemoglobin < 10 g/dL  
2. Pretreatment serum erythropoietin level < 500 mU/mL

F. **Anemia Due to Cancer**  
Authorization of 12 weeks may be granted for members who have cancer and are undergoing palliative treatment

### III. CONTINUATION OF THERAPY

Note: Requirements regarding pretreatment hemoglobin level exclude values due to a recent transfusion. Members may not use Aranesp concomitantly with other erythropoiesis stimulating agents.

**For all indications below:** all members (including new members) requesting authorization for continuation of therapy after at least 12 weeks of ESA treatment must show a response with a rise in hemoglobin of ≥ 1 g/dL. Members who completed less than 12 weeks of ESA treatment and have not yet responded with a rise in hemoglobin of ≥ 1 g/dL may be granted authorization of up to 12 weeks to allow for sufficient time to demonstrate a response.

A. **Anemia due to CKD**  
Authorization of 12 weeks may be granted for continuation of treatment when the current hemoglobin is ≤ 12 g/dL.

B. **Anemia Due to Myelosuppressive Chemotherapy**  
Authorization of 12 weeks may be granted for continuation of treatment in members with nonmyeloid malignancy when the current hemoglobin is < 12 g/dL.

C. **Anemia in MDS**  
Authorization of 12 weeks may be granted for continuation of treatment when the current hemoglobin is ≤ 12 g/dL.

D. **Anemia in members whose religious beliefs forbid blood transfusions**  
Authorization of 12 weeks may be granted for continuation of treatment when the current hemoglobin is ≤ 12 g/dL.

E. **Anemia in Primary Myelofibrosis, Post-polycythemia Vera Myelofibrosis, and Post-Essential Thrombocythemia Myelofibrosis**  
Authorization of 12 weeks may be granted for continuation of treatment when the current hemoglobin is ≤ 12 g/dL.

F. **Anemia Due to Cancer**  
Authorization of 12 weeks may be granted for members who have cancer and are undergoing palliative treatment

### IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

ARCALYST (rilonacept)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   Treatment of Cryopyrin Associated Periodic Syndromes (CAPS), including Familial Cold Auto-inflamatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS) in adults and children 12 years of age and older.

B. Compendial Uses
   Prevention of gout flares in patients initiating or continuing urate-lowering therapy

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Cryopyrin-Associated Periodic Syndrome (CAPS)
   Authorization of 24 months may be granted for treatment of CAPS, including FCAS and MWS.

B. Prevention of Gout Flares in Members Initiating or Continuing Urate-Lowering Therapy
   Authorization of 4 months may be granted for the prevention of gout flares when initiating or continuing urate-lowering therapy when ALL of the following criteria are met:
   1. Member had two or more gout flares within the previous 12 months
   2. Member had an inadequate response, intolerance or contraindication to maximum tolerated doses of non-steroidal anti-inflammatory drugs and colchicine
   3. Member will receive Arcalyst concurrently with urate-lowering therapy (i.e., allopurinol or febuxostat)

III. CONTINUATION OF THERAPY

A. Cryopyrin-Associated Periodic Syndrome (CAPS)
   All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria.

B. Prevention of Gout Flares in Members Initiating or Continuing Urate-Lowering Therapy
   Authorization of 4 months may be granted to members who meet ALL of the following criteria:
   1. Member has achieved or maintained a clinical benefit (i.e., a fewer number of gout attacks or fewer flare days) compared to baseline
   2. Member will receive Arcalyst concurrently with urate-lowering therapy (i.e., allopurinol or febuxostat)
IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

ARZERRA (ofatumumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   Chronic lymphocytic leukemia (CLL):
   1. Arzerra is indicated in combination with chlorambucil, for the treatment of previously untreated patients with CLL for whom fludarabine-based therapy is considered inappropriate.
   2. Arzerra is indicated in combination with fludarabine and cyclophosphamide for the treatment of patients with relapsed CLL.
   3. Arzerra is indicated for extended treatment of patients who are in complete or partial response after at least two lines of therapy for recurrent or progressive CLL.
   4. Arzerra is indicated for the treatment of patients with CLL refractory to fludarabine and alemtuzumab.

B. Compendial Uses
   1. First-line treatment of CLL
   2. Small lymphocytic lymphoma (SLL) (managed in the same manner as CLL)
   3. Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Chronic Lymphocytic Leukemia (CLL) and Small Lymphocytic Lymphoma (SLL)
   Authorization of 12 months may be granted for the treatment of CD20-positive CLL or SLL.

B. Waldenström’s Macroglobulinemia/Lymphoplasmacytic Lymphoma
   Authorization of 12 months may be granted for the treatment of CD20-positive Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

ASPARLAS (calaspargase pegol - mknl)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Asparlas is indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of acute lymphoblastic leukemia in pediatric and young adult patients age 1 month to 21 years.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for the treatment of acute lymphoblastic leukemia when all of the following criteria are met:
A. Asparlas will be used in conjunction with multi-agent chemotherapy.
B. The member is age 1 month to 21 years.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

AUBAGIO (teriflunomide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication: Aubagio is indicated for the treatment of patients with relapsing forms of multiple sclerosis.

All other indications are considered experimental/investigational and are not covered benefits.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with a relapsing form of multiple sclerosis who are experiencing disease stability or improvement while receiving Aubagio.

IV. OTHER CRITERIA

Members will not use Aubagio concomitantly with other medications used for the treatment of multiple sclerosis, excluding Ampyra.

V. REFERENCE

SPECIALTY GUIDELINE MANAGEMENT

AUSTEDO (deutetrabenazine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
1. Treatment of chorea associated with Huntington’s disease
2. Treatment of tardive dyskinesia in adults

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR APPROVAL

Chorea associated with Huntington disease
Authorization of 12 months may be granted for treatment of chorea associated with Huntington disease.

Tardive dyskinesia
Authorization of 12 months may be granted for treatment of tardive dyskinesia.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

AVASTIN (bevacizumab)
MVASI (bevacizumab-awwb)
ZIRABEV (bevacizumab-bvzr)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Metastatic colorectal cancer (mCRC)
   a. Avastin, in combination with intravenous 5-fluorouracil-based chemotherapy, is indicated for the first- or second-line treatment of patients with metastatic colorectal cancer.
   b. Avastin, in combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy, is indicated for the second-line treatment of patients with metastatic colorectal cancer who have progressed on a first-line Avastin-containing regimen.

2. First-line non-squamous non-small cell lung cancer (NSCLC)
   Avastin, in combination with carboplatin and paclitaxel, is indicated for the first-line treatment of patients with unresectable, locally advanced, recurrent or metastatic non–squamous non–small cell lung cancer.

3. Recurrent glioblastoma (RGM)
   Avastin is indicated for the treatment of recurrent glioblastoma in adults.

4. Metastatic renal cell carcinoma (mRCC)
   Avastin, in combination with interferon alfa, is indicated for the treatment of metastatic renal cell carcinoma.

5. Persistent, recurrent, or metastatic cervical cancer
   Avastin, in combination with carboplatin and paclitaxel and paclitaxel and topotecan, is indicated for the treatment of patients with persistent, recurrent, or metastatic cervical cancer.

6. Epithelial ovarian, fallopian tube, or primary peritoneal cancer
   a. Avastin, in combination with carboplatin and paclitaxel, followed by Avastin as a single agent, is indicated for the treatment of patients with stage III or IV epithelial ovarian, fallopian tube, or primary peritoneal cancer following initial surgical resection.
   b. Avastin, in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan, is indicated for the treatment of patients with platinum-resistant recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer who received no more than 2 prior chemotherapy regimens.
   c. Avastin, in combination with carboplatin and paclitaxel, or with carboplatin and gemcitabine, followed by Avastin as a single agent, is indicated for the treatment of patients with platinum-sensitive recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer.

B. Compendial Uses

1. Breast cancer for recurrent or stage IV (M1) human epidermal growth factor receptor 2 (HER2)-negative disease

2. Central nervous system (CNS) cancers
   a. Adult low-grade (WHO Grade II) infiltrative supratentorial astrocytoma/oligodendroglioma
   b. Adult intracranial and spinal ependymoma (excluding subependymoma)
   c. Anaplastic gliomas
   d. Adult medulloblastoma
e. Primary central nervous system lymphoma
f. Meningiomas
g. Limited and extensive brain metastases
h. Leptomeningeal metastases
i. Metastatic spine tumors
3. Malignant pleural mesothelioma
4. Ovarian cancer/Fallopian tube cancer/Primary peritoneal cancer
   a. Carcinosarcoma (malignant mixed Mullerian tumors)
   b. Clear cell carcinoma
   c. Mucinous carcinoma
   d. Low-grade serous/grade 1 endometrioid epithelial carcinoma
e. Malignant sex cord-stromal tumors
5. Soft tissue sarcoma
   a. Angiosarcoma
   b. Solitary fibrous tumor/Hemangiopericytoma
6. AIDS-related Kaposi sarcoma
7. Uterine/Endometrial cancer
8. Vulvar cancer
9. Ophthalmic disorders
   a. Diabetic macular edema
   b. Neovascular (wet) age-related macular degeneration (AMD)
   c. Macular edema following retinal vein occlusion (RVO)
   d. Proliferative diabetic retinopathy
   e. Choroidal neovascularization (CNV)
   f. Neovascular glaucoma; adjunct
   g. Retinopathy of prematurity

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Ophthalmic disorders
   Authorization of 24 months may be granted for the following retinal disorders:
   1. Diabetic macular edema
   2. Neovascular (wet) age-related macular degeneration including subtypes:
      a. Polypoidal choroidopathy
      b. Retinal angiomatous proliferation
   3. Macular edema following retinal vein occlusion
   4. Proliferative diabetic retinopathy
   5. Choroidal neovascularization
   6. Neovascular glaucoma
   7. Retinopathy of prematurity

B. Colorectal cancer (CRC)
   Authorization of 12 months may be granted for the treatment of colorectal cancer.

C. Non-small cell lung cancer (NSCLC)
   Authorization of 12 months may be granted for the treatment of non-squamous NSCLC.

D. CNS cancer
   Authorization of 12 months may be granted for treatment of the following types of CNS cancer:
   1. Glioblastoma
2. Adult intracranial and spinal ependymoma (excludes subependymoma)
3. Anaplastic glioma
4. Adult low-grade (WHO Grade II) infiltrative supratentorial astrocytoma/oligodendroglioma
5. Adult medulloblastoma
6. Primary central nervous system lymphoma
7. Meningiomas
8. Limited and extensive brain metastases
9. Leptomeningeal metastases
10. Metastatic spine tumors

E. Ovarian cancer/Fallopian tube cancer/Primary peritoneal cancer
- Authorization of 12 months may be granted for the treatment of the following types of ovarian fallopian tube cancer/primary peritoneal cancer:
  1. Epithelial ovarian cancer
  2. Fallopian tube cancer
  3. Primary peritoneal cancer
  4. Carcinosarcoma (malignant mixed Müllerian tumors)
  5. Clear cell carcinoma
  6. Mucinous carcinoma
  7. Low-grade serous/grade 1 endometrioid epithelial carcinoma
  8. Malignant sex cord-stromal tumors

F. Uterine/Endometrial cancer
- Authorization of 12 months may be granted for the treatment of uterine cancer or endometrial cancer.

G. Cervical cancer
- Authorization of 12 months may be granted for the treatment of cervical cancer.

H. Breast cancer
- Authorization of 12 months may be granted for treatment of breast cancer.

I. Renal cell carcinoma
- Authorization of 12 months may be granted for the treatment of renal cell carcinoma.

J. Soft tissue sarcoma
- Authorization of 12 months may be granted for the treatment of the following types of soft tissue sarcoma:
  1. AIDS-related Kaposi sarcoma
  2. Angiosarcoma
  3. Solitary fibrous tumor/hemangiopericytoma

K. Malignant Pleural Mesothelioma
- Authorization of 12 months may be granted for the treatment of malignant pleural mesothelioma.

L. AIDS-related Kaposi sarcoma
- Authorization of 12 months may be granted for the treatment of AIDS-related Kaposi sarcoma.

M. Vulvar cancer
- Authorization of 12 months may be granted for the treatment of vulvar cancer.

III. CONTINUATION OF THERAPY
All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

AVEED (testosterone undecanoate injection)

POLICY

I. INDICATION

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Aveed is indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone.
1. Primary hypogonadism (congenital or acquired): testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter's syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations and gonadotropins (follicle-stimulating hormone [FSH], luteinizing hormone [LH]) above the normal range.
2. Hypogonadotropic hypogonadism (congenital or acquired): gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations but have gonadotropins in the normal or low range.

Aveed should only be used in patients who require testosterone replacement therapy and in whom the benefits of the product outweigh the serious risks of pulmonary oil microembolism and anaphylaxis.

Limitations of use:
• Safety and efficacy of Aveed in men with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.
• Safety and efficacy of Aveed in males less than 18 years old have not been established.

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review: Pretreatment morning serum total testosterone concentrations

III. EXCLUSIONS

Coverage will not be provided for members with any of the following exclusions: Use for age-related hypogonadism or late-onset hypogonadism

IV. CRITERIA FOR INITIAL APPROVAL
Primary hypogonadism or hypogonadotropic hypogonadism

Authorization of 12 months may be granted for treatment of primary hypogonadism or hypogonadotropic hypogonadism when all of the following criteria are met:
1. Member is a biological male or a person that self identifies as male.
2. Member is at least 18 years of age.
3. Member has at least two confirmed low morning serum total testosterone concentrations based on the reference laboratory range or current practice guidelines.

V. CONTINUATION OF THERAPY

For members requesting authorization for continuation of therapy with primary hypogonadism or hypogonadotropic hypogonadism who are not currently receiving Aveed therapy through samples or a manufacturer’s patient assistance program, authorization of 12 months may be granted if the member meets criteria IV.1 and IV.2 above. All other members (including new members) must meet all initial authorization criteria.

VI. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

AVONEX (interferon beta-1a)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Avonex is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

All other indications are considered experimental/investigational and are not covered benefits.

II. CRITERIA FOR INITIAL APPROVAL

A. Relapsing forms of multiple sclerosis
Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

B. Clinically isolated syndrome
Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome of multiple sclerosis.

III. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted for members who are experiencing disease stability or improvement while receiving Avonex.

IV. OTHER CRITERIA

Members will not use Avonex concomitantly with other medications used for the treatment of multiple sclerosis, excluding Ampyra.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

VIDAZA (azacitidine)
azacitidine (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Myelodysplastic syndromes (MDS): Vidaza is indicated for treatment of patients with the following French-American-British (FAB) myelodysplastic syndrome subtypes: refractory anemia (RA) or refractory anemia with ringed sideroblasts (if accompanied by neutropenia or thrombocytopenia or requiring transfusions), refractory anemia with excess blasts (RAEB), refractory anemia with excess blasts in transformation (RAEB-T), and chronic myelomonocytic leukemia (CMMoL).

B. Compendial Uses

1. Acute myeloid leukemia (AML)
2. Accelerated phase or blast phase myelofibrosis

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Myelodysplastic Syndromes (MDS)

Authorization of 12 months may be granted for the treatment of MDS.

B. Acute Myeloid Leukemia (AML)

Authorization of 12 months may be granted for the treatment of AML.

C. Accelerated Phase or Blast Phase Myelofibrosis

Authorization of 12 months may be granted for the treatment of accelerated phase or blast phase myelofibrosis.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

BALVERSA (erdafitinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Balversa is indicated for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma (mUC), that has:
1. susceptible FGFR3 or FGFR2 genetic alterations, and
2. progressed during or following at least one line of prior platinum-containing chemotherapy, including within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy.

Select patients for therapy based on an FDA-approved companion diagnostic for Balversa. This indication is approved under accelerated approval based on tumor response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Fibroblast growth factor receptor (FGFR)3 or FGFR2 mutation status

III. CRITERIA FOR INITIAL APPROVAL

Urothelial carcinoma
Authorization of 12 months may be granted for treatment of locally advanced or metastatic urothelial carcinoma when both of the following criteria are met:
1. Member has a susceptible FGFR3 or FGFR2 genetic alteration.
2. Disease progressed during or following at least one line of prior platinum-containing chemotherapy, including within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced disease progression or an unacceptable toxicity.
V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

BAVENCIO (avelumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
A. Metastatic Merkel Cell Carcinoma
   Treatment of adults and pediatric patients 12 years and older with metastatic Merkel cell carcinoma
B. Locally Advanced or Metastatic Urothelial Carcinoma
   Treatment of patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy
C. Advanced Renal Cell Carcinoma
   First-line treatment of patients with advanced renal cell carcinoma in combination with axitinib

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Merkel Cell Carcinoma
   Authorization of 12 months may be granted for the treatment of metastatic Merkel cell carcinoma.

B. Urothelial Carcinoma
   Authorization of 12 months may be granted for treatment of locally advanced or metastatic urothelial carcinoma when either of the following criteria are met:
   1. Member experienced disease progression during or following platinum-containing chemotherapy.
   2. Member experienced disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

C. Renal Cell Carcinoma
   Authorization of 12 months may be granted for treatment of advanced renal cell carcinoma when Bavencio is given in combination with axitinib as first-line treatment for the disease.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

BELEODAQ (belinostat)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
   Treatment of patients with relapsed or refractory peripheral T-cell lymphoma (PTCL)

B. Compendial Uses
   Non-Hodgkin’s Lymphoma (NHL)
   1. Adult T-cell leukemia/lymphoma (ATLL)
   2. Mycosis fungoides (MF)/Sezary syndrome (SS)
   3. Primary cutaneous CD30+ T-cell lymphoproliferative disorders: cutaneous anaplastic large cell lymphoma
   4. Extranodal NK/T-cell lymphoma, nasal type
   5. Hepatosplenic gamma-delta T-cell lymphoma

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Peripheral T-cell lymphoma (PTCL)
   Authorization of 12 months may be granted for treatment of PTCL when used for relapsed or refractory disease.

B. Adult T-cell leukemia/lymphoma (ATLL)
   Authorization of 12 months may be granted for treatment of ATLL when both of the following criteria are met:
   1. Beleodaq is used as a single agent.
   2. Beleodaq is used for second-line or subsequent therapy.

C. Mycosis fungoides (MF)/Sezary syndrome (SS)
   Authorization of 12 months may be granted for treatment of mycosis fungoides (MF)/Sezary syndrome (SS).

D. Primary cutaneous CD30+ T-cell lymphoproliferative disorders
   Authorization of 12 months may be granted for treatment of cutaneous anaplastic large cell lymphoma (ALCL) when both of the following criteria are met:
   1. Beleodaq is used as a single agent, and
   2. The disease is relapsed or refractory
E. **Extranodal NK/T-cell lymphoma, nasal type**
   Authorization of 12 months may be granted for treatment of extranodal NK/T-cell lymphoma, nasal type when all of the following criteria are met:
   1. Beleodaq will be used as a single agent.
   2. Patient has relapsed or refractory disease.
   3. Patient has had an inadequate response or contraindication to asparaginase-based therapy (e.g., pegaspargase).

F. **Hepatosplenic gamma-delta T-cell lymphoma**
   Authorization of 12 months may be granted for treatment of hepatosplenic gamma-delta T-cell lymphoma when both of the following are met:
   1. Beleodaq will be used a single agent.
   2. The patient has had two or more previous lines of chemotherapy.

III. **CONTINUATION OF THERAPY**

   Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. **REFERENCES**
      Available at: [https://www.nccn.org](https://www.nccn.org) Accessed April 18, 2019.
SPECIALTY GUIDELINE MANAGEMENT

BENLYSTA (belimumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Treatment of adult patients with active, autoantibody-positive, systemic lupus erythematosus (SLE) who are receiving standard therapy.

Limitations of Use
The efficacy of Benlysta has not been evaluated in patients with severe active lupus nephritis or severe active central nervous system lupus. Benlysta has not been studied in combination with other biologics or intravenous cyclophosphamide. Use of Benlysta is not recommended in these situations.

All other indications are considered experimental/investigational and are not a covered benefit.

II. EXCLUSIONS

Coverage will not be provided for members with any of the following exclusions:

A. Severe active lupus nephritis
B. Severe active central nervous system lupus

III. CRITERIA FOR INITIAL APPROVAL

Systemic Lupus Erythematosus (SLE)
Authorization of 24 months may be granted for treatment of active SLE when all of the following criteria are met:

A. Prior to initiating therapy, the member is positive for autoantibodies relevant to SLE (e.g., anti-nuclear antibody or anti-double-stranded DNA antibody).
B. The member is currently receiving standard therapy for SLE (see Appendix) or has tried and had an inadequate response or intolerance to standard therapy for SLE.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.
V. APPENDIX

Examples of Standard Therapy for SLE
- Antimalarials (e.g., hydroxychloroquine)
- Azathioprine
- Corticosteroids
- Leflunomide
- Methotrexate
- Mycophenolate mofetil
- Non-steroidal anti-inflammatory drugs

VI. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

BERINERT (C1 esterase inhibitor [human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Treatment of acute abdominal, facial, or laryngeal attacks of hereditary angioedema (HAE) in adult and pediatric patients

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. C4 levels and C1 inhibitor functional and antigenic protein levels
B. F12, angiopoietin-1 or plasminogen gene mutation testing, if applicable
C. Chart notes confirming family history of angioedema, if applicable

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of hereditary angioedema attacks when the medication will not be used with Firazyr, Kalbitor, or Ruconest and either of the following criteria is met:

A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing:
   1. C1 inhibitor (C1-INH) antigenic level below the lower limit of normal as defined by the laboratory performing the test; or
   2. Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test)
B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
   1. Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing, or
   2. Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy when all of the following criteria are met:

A. Member meets the criteria for initial approval.
B. Member has experienced reduction in severity and/or duration of attacks when they use Berinert to treat an acute attack.
V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

BERINERT (C1 esterase inhibitor [human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Treatment of acute abdominal, facial, or laryngeal attacks of hereditary angioedema (HAE) in adult and pediatric patients.

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. C4 levels and C1 inhibitor functional and antigenic protein levels
B. F12, angiopoietin-1 or plasminogen gene mutation testing, if applicable
C. Chart notes confirming family history of angioedema, if applicable

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of hereditary angioedema attacks when the medication will not be used with Firazyr, Kalbitor, or Ruconest and either of the following criteria is met:
A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing:
   1. C1 inhibitor (C1-INH) antigenic level below the lower limit of normal as defined by the laboratory performing the test; or
   2. Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test)
B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
   1. Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing, or
   2. Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy when all of the following criteria are met:
A. Member meets the criteria for initial approval.
B. Member has experienced reduction in severity and/or duration of attacks when they use Berinert to treat an acute attack.
V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

BESPONSA (inotuzumab ozogamicin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Besponsa is indicated for the treatment of adults with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Testing or analysis confirming CD22 protein on the surface of the B-cell.

III. CRITERIA FOR INITIAL APPROVAL

Acute lymphoblastic leukemia (ALL)

Authorization of 12 months may be granted for treatment of relapsed or refractory ALL when all of the following criteria are met:

A. Member has B-cell precursor ALL.
B. The tumor is CD22-positive as confirmed by testing or analysis to identify the CD22 protein on the surface of the B-cell.
C. Member meets one of the following:
   1. Member has Philadelphia chromosome-positive disease and is intolerant or refractory to tyrosine kinase inhibitor therapy (e.g., imatinib, dasatinib, nilotinib, bosutinib, ponatinib).
   2. Member has Philadelphia chromosome-negative disease.
D. Member will not receive more than 6 treatment cycles of Besponsa.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

BETASERON (interferon beta-1b)
EXTAVIA (interferon beta-1b)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications: Betaseron and Extavia are indicated for the treatment of relapsing forms of multiple sclerosis to reduce the frequency of clinical exacerbations. Patients with multiple sclerosis in whom efficacy has been demonstrated include patients who have experienced a first clinical episode and have MRI features consistent with multiple sclerosis.

All other indications are considered experimental/investigational and are not covered benefits.

II. CRITERIA FOR INITIAL APPROVAL

A. Relapsing forms of multiple sclerosis
   Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis.

B. First clinical episode of multiple sclerosis
   Authorization of 12 months may be granted to members for the treatment of a first clinical episode of multiple sclerosis.

III. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted for members who are experiencing disease stability or improvement while receiving Betaseron or Extavia.

IV. OTHER CRITERIA

Members will not use Betaseron or Extavia concomitantly with other medications used for the treatment of multiple sclerosis, excluding Ampyra.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

Targretin (bexarotene) capsules
bexarotene capsules (generic)
Targretin (bexarotene) gel 1%

POLICY

I. INDICATIONS
The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Targretin/bexarotene capsules are indicated for the treatment of cutaneous manifestations of cutaneous T-cell lymphoma (CTCL) in patients who are refractory to at least one prior systemic therapy.
2. Targretin gel is indicated for the topical treatment of cutaneous lesions in patients with CTCL (Stage IA and IB) who have refractory or persistent disease after other therapies or who have not tolerated other therapies.

B. Compendial Uses
1. Targretin/bexarotene capsules
   i. Mycosis fungoides (MF)
   ii. Sézary syndrome (SS)
   iii. Primary cutaneous CD30+ T-cell lymphoproliferative disorders:
      a. Primary cutaneous anaplastic large cell lymphoma (ALCL)
      b. Lymphomatoid papulosis (LyP)
2. Targretin gel
   i. Mycosis fungoides (MF)
   ii. Chronic or smoldering adult T-cell leukemia/lymphoma (ATLL)
   iii. Primary cutaneous B-cell lymphoma:
      a. Primary cutaneous marginal zone lymphoma
      b. Primary cutaneous follicle center lymphoma

All other indications are considered experimental/investigational and are not covered benefits.

II. CRITERIA FOR INITIAL APPROVAL

A. Targretin/bexarotene Capsules
1. Mycosis Fungoides (MF)/Sézary Syndrome (SS)
   Authorization of 12 months may be granted for the treatment of MF or SS.

2. Primary Cutaneous Anaplastic Large Cell Lymphoma (ALCL)/Lymphomatoid Papulosis (LyP)
   Authorization of 12 months may be granted for the treatment of primary cutaneous ALCL or LyP.

B. Targretin Gel
1. Cutaneous T-cell Lymphoma (CTCL): Mycosis Fungoides (MF) (excluding Sézary syndrome)
Authorization of 12 months may be granted for the treatment of MF.

2. **Adult T-cell Leukemia/Lymphoma (ATLL)**
   Authorization of 12 months may be granted for the treatment of chronic or smoldering ATLL.

3. **Primary Cutaneous B-cell Lymphoma**
   Authorization of 12 months may be granted for the treatment of primary cutaneous marginal zone lymphoma or primary cutaneous follicle center lymphoma.

III. **CONTINUATION OF THERAPY**

All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria.

IV. **REFERENCES**

SPECIALTY GUIDELINE MANAGEMENT

BLINCYTO (blinatumomab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
1. Blincyto is indicated for the treatment of B-cell precursor acute lymphoblastic leukemia (ALL) in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1% in adults and children.
2. Blincyto is indicated for the treatment of relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL) in adults and children.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

B-cell Precursor Acute Lymphoblastic Leukemia
Authorization of 9 months may be granted for treatment of B-cell precursor acute lymphoblastic leukemia (ALL).

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

VELCADE (bortezomib) bortezomib

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Multiple myeloma
   2. Mantle cell lymphoma

B. Compendial Uses
   1. Systemic light chain amyloidosis
   2. Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma
   3. Multicentric Castleman’s disease
   4. Adult T-cell leukemia/lymphoma
   5. Primary cutaneous anaplastic large cell lymphoma

All other indications are considered experimental/investigational and are not covered benefits.

II. CRITERIA FOR INITIAL APPROVAL

A. Multiple myeloma
   Authorization of 12 months may be granted for the treatment of multiple myeloma.

B. Mantle cell lymphoma
   Authorization of 12 months may be granted for the treatment of mantle cell lymphoma.

C. Multicentric Castleman’s disease
   Authorization of 12 months may be granted for the treatment of multicentric Castleman’s disease.

D. Systemic light chain amyloidosis
   Authorization of 12 months may be granted for the treatment of systemic light chain amyloidosis.

E. Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma
   Authorization of 12 months may be granted for the treatment of Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma.

F. Adult T-cell Leukemia/Lymphoma
   Authorization of 12 months may be granted for the treatment of adult T-cell leukemia/lymphoma.

G. Primary cutaneous anaplastic large cell lymphoma
   Authorization of 12 months may be granted for the treatment of primary cutaneous anaplastic large cell lymphoma (ALCL).
III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

TRACLEER (bosentan)
bosentan

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
A. In adults to improve exercise ability and to decrease clinical worsening.
B. In pediatric patients aged 3 years and older with idiopathic or congenital PAH to improve pulmonary vascular resistance (PVR), which is expected to result in an improvement in exercise ability.

All other indications are considered experimental/investigational and are not a covered benefit.

Compendial Use
Eisenmenger’s syndrome, WHO functional class III PAH

II. CRITERIA FOR INITIAL APPROVAL

A. Pulmonary Arterial Hypertension (PAH)
Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:
1. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
2. PAH was confirmed by either criterion (1) or criterion (2) below:
   a. Pretreatment right heart catheterization with all of the following results:
      i. mPAP ≥ 25 mmHg
      ii. PCWP ≤ 15 mmHg
      iii. PVR > 3 Wood units
   b. For infants less than one year of age with any of the following conditions, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed:
      i. Post cardiac surgery
      ii. Chronic heart disease
      iii. Chronic lung disease associated with prematurity
      iv. Congenital diaphragmatic hernia

B. Eisenmenger’s Syndrome
Authorization of 12 months may be granted for treatment of members with WHO functional class III Eisenmenger’s syndrome (refer to Appendix).
III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section II who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. APPENDIX

WHO Classification of Pulmonary Hypertension

1 PAH
1.1 Idiopathic (PAH)
1.2 Heritable PAH
1.3 Drug- and toxin-induced PAH
1.4. PAH associated with:
   1.4.1 Connective tissue diseases
   1.4.2 HIV infection
   1.4.3 Portal hypertension
   1.4.4 Congenital heart diseases
   1.4.5 Schistosomiasis
1.5 PAH long-term responders to calcium channel blockers
1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease
2.1 PH due to heart failure with preserved LVEF
2.2 PH due to heart failure with reduced LVEF
2.3 Valvular heart disease
2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia
3.1 Obstructive lung disease
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction
4.1 Chronic thromboembolic PH
4.2 Other pulmonary artery obstructions
   4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
   4.2.2 Other malignant tumors
      Renal carcinoma
      Uterine carcinoma
      Germ cell tumours of the testis
      Other tumours
   4.2.3 Non-malignant tumours
      Uterine leiomyoma
   4.2.4 Arteritis without connective tissue disease
   4.2.5 Congenital pulmonary artery stenosis
   4.2.6 Parasites
      Hydatidosis

5 PH with unclear and/or multifactorial mechanisms
5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
5.4 Complex congenital heart disease

WHO Functional Assessment for Pulmonary Hypertension
Class I
Patients with pulmonary hypertension but without resulting limitation of physical activity. Ordinary physical activity does not cause undue dyspnea or fatigue, chest pain or near syncope.

Class II
Patients with pulmonary hypertension resulting in a slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity causes undue dyspnea or fatigue, chest pain or near syncope.

Class III
Patients with pulmonary hypertension resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes undue dyspnea or fatigue, chest pain or near syncope.

Class IV
Patients with pulmonary hypertension with inability to carry out any physical activity without symptoms. These patients manifest signs of right heart failure. Dyspnea and/or fatigue may even be present at rest. Discomfort is increased by any physical activity.

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

BOSULIF (bosutinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   Adult patients with:
   1. Newly-diagnosed chronic phase (CP) Philadelphia chromosome-positive chronic myelogenous leukemia (Ph+ CML)
   2. Chronic phase, accelerated phase (AP), or blast phase (BP) Ph+ CML with resistance or intolerance to prior therapy

B. Compendial Uses
   1. Primary treatment of patients with advanced phase CML (accelerated phase or blast phase)
   2. Follow-up therapy for CML patients after hematopoietic stem cell transplant (HSCT)
   3. Therapy for relapsed or refractory Ph+ acute lymphoblastic leukemia (ALL)

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review:

A. Prior to initiation of therapy: results of cytogenetic and/or molecular testing for detection of the Ph chromosome or the BCR-ABL gene

B. For members requesting initiation of Bosulif therapy for treatment of CML or ALL after experiencing resistance to prior tyrosine kinase inhibitor (TKI) therapy: results of T315I mutation testing

III. CRITERIA FOR INITIAL APPROVAL

A. Chronic Myeloid Leukemia (CML)
   Authorization of 6 months may be granted for treatment of CML that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when any of the following criteria are met:
   1. Member has not received prior therapy with a TKI (e.g., dasatinib, imatinib, nilotinib, ponatinib)
   2. Member experienced toxicity or intolerance to prior therapy with a TKI
   3. Member experienced resistance to prior therapy with a TKI and results of mutational testing are negative for T315I mutation
   4. Member has received HSCT for CML

B. Ph+ Acute Lymphoblastic Leukemia (ALL)/Lymphoblastic Lymphoma (LL)
Authorization of 12 months may be granted for treatment of relapsed or refractory Ph+ ALL or LL that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when results of mutational testing are negative for T315I mutation.

IV. CONTINUATION OF THERAPY

A. CML

Authorization of 12 months may be granted for continued treatment of CML that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when either of the following criteria are met:
1. BCR-ABL1 ≤ 10% for members who have been receiving Bosulif for ≤ 12 months
2. No evidence of disease progression for members who have been receiving Bosulif for > 12 months
3. Member has received HSCT

B. Ph+ ALL/LL

Authorization of 12 months may be granted for continued treatment of Ph+ ALL or LL that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing in members who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

BOTOX (onabotulinumtoxinA)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Overactive bladder with symptoms of urge urinary incontinence, urgency, and frequency, in adults who have an inadequate response to or are intolerant of an anticholinergic medication
   2. Urinary incontinence due to detrusor overactivity associated with a neurologic condition (e.g., spinal cord injury, multiple sclerosis) in adults who have an inadequate response to or are intolerant of an anticholinergic medication
   3. Prophylaxis of headaches in adult patients with chronic migraine (≥15 days per month with headache lasting 4 hours a day or longer)
   4. Treatment of upper limb spasticity in adult patients
   5. Treatment of lower limb spasticity in adult patients
   6. Cervical dystonia in adults, to reduce the severity of abnormal head position and neck pain
   7. Severe primary axillary hyperhidrosis that is inadequately managed with topical agents in adult patients
   8. Strabismus and blepharospasm associated with dystonia, including benign essential blepharospasm or VII nerve disorders in patients 12 years of age and above

B. Compendial Uses
   1. Achalasia
   2. Chronic anal fissures
   3. Essential tremor
   4. Excessive salivation secondary to advanced Parkinson's disease
   5. Hemifacial spasm
   6. Spasmodic dysphonia (laryngeal dystonia)

All other indications are considered experimental/investigational and are not a covered benefit.

II. EXCLUSIONS

Coverage will not be provided for cosmetic use.

III. CRITERIA FOR INITIAL APPROVAL

A. Blepharospasm
   Authorization of 24 months may be granted for treatment of blepharospasm.
B. **Cervical dystonia**
   Authorization of 24 months may be granted for treatment of cervical dystonia (e.g., torticollis).

C. **Chronic migraine prophylaxis**
   Authorization of 6 months (two injection cycles) may be granted for treatment of chronic migraine prophylaxis when all of the following criteria are met:
   1. Member experiences headaches ≥ 15 days per month
   2. Member completed adequate trial (≥ 8 weeks) of an oral migraine preventative therapy such as:
      a. Divalproex sodium (Depakote, Depakote ER)
      b. Topiramate (Topamax)
      c. Gabapentin (Neurontin)
      d. Amitriptyline (Elavil)
      e. Venlafaxine (Effexor)
      f. Atenolol/Metoprolol/Propranolol/Timolol/Nadolol
      g. Nimodipine/Verapamil
      h. Naproxen/other NSAID

D. **Overactive bladder with urinary incontinence**
   Authorization of 12 months may be granted for treatment of overactive bladder with urinary incontinence when the member has an inadequate response or experienced intolerance to an anticholinergic medication (e.g., Vesicare [solifenacin], Enablex [darifenacin], Toviaz [fesoterodine], Detrol/Detrol LA [tolterodine], Sanctura/Sanctura XR [trosperim], Ditropan XL [oxybutynin]).

E. **Primary axillary hyperhidrosis**
   Authorization of 12 months may be granted for treatment of primary axillary hyperhidrosis.

F. **Strabismus**
   Authorization of 12 months may be granted for treatment of strabismus.

G. **Upper limb spasticity**
   Authorization of 24 months may be granted for treatment of upper limb spasticity.

H. **Lower limb spasticity**
   Authorization of 24 months may be granted for treatment of lower limb spasticity.

I. **Urinary incontinence associated with a neurologic condition (e.g., spinal cord injury, multiple sclerosis)**
   Authorization of 24 months may be granted for treatment of urinary incontinence associated with a neurologic condition (e.g., spinal cord injury, multiple sclerosis) when the member has an inadequate response or experienced intolerance to an anticholinergic medication (e.g., Vesicare [solifenacin], Enablex [darifenacin], Toviaz [fesoterodine], Detrol/Detrol LA [tolterodine], Sanctura/Sanctura XR [trosperim], Ditropan XL [oxybutynin]).

J. **Achalasia**
   Authorization of 24 months may be granted for treatment of achalasia.

K. **Chronic anal fissures**
   Authorization of 12 months may be granted for treatment of chronic anal fissures.

L. **Essential tremor**
Authorization of 24 months may be granted for treatment of essential tremor.

M. Excessive salivation due to advanced Parkinson’s disease
Authorization of 24 months may be granted for treatment of excessive salivation due to advanced Parkinson’s disease.

N. Hemifacial spasm
Authorization of 24 months may be granted for treatment of hemifacial spasm.

O. Spasmodic dysphonia (laryngeal dystonia)
Authorization of 24 months may be granted for treatment of spasmodic dysphonia (laryngeal dystonia).

IV. CONTINUATION OF THERAPY

A. All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria for all approvable conditions other than chronic migraine prophylaxis.

B. Authorization of 12 months may be granted for treatment of chronic migraine prophylaxis when the member has achieved or maintained a 50% reduction in monthly headache frequency since starting therapy with Botox.

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

BRAFTOVI (encorafenib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Braftovi is indicated, in combination with binimetinib, for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, as detected by an FDA-approved test.

Limitations of use: Braftovi is not indicated for treatment of patients with wild-type BRAF melanoma.

B. Compendial Uses

1. Glioma, BRAF V600 activating mutation-positive
2. Meningioma, BRAF V600 activating mutation-positive
3. Astrocytoma, BRAF V600 activating mutation-positive
4. Colorectal cancer, BRAF V600E activating mutation-positive

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of BRAF mutation documentation is necessary to initiate the prior authorization review.

III. CRITERIA FOR INITIAL APPROVAL

A. Melanoma

Authorization of 12 months may be granted for treatment of unresectable or metastatic melanoma when all of the following criteria are met:
1. Braftovi is used in combination with binimetinib (Mektovi)
2. Tumor is positive for BRAF V600E or V600K mutation.

B. Central Nervous System Cancer

Authorization of 12 months may be granted for treatment of BRAF V600 mutation-positive gliomas, meningiomas, or astrocytomas.

C. Colorectal Cancer

Authorization of 12 months may be granted for treatment of unresectable advanced or metastatic colorectal cancer when the following criteria are met:
1. Braftovi is used in combination with binimetinib (Mektovi) and either cetuximab or panitumumab
2. Tumor is positive for BRAF V600E mutation.
3. Will be used as subsequent therapy
IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in section III when there is no evidence of unacceptable toxicity or disease progression on the current regimen.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

BRINEURA (cerliponase alfa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Brineura is indicated to slow the loss of ambulation in symptomatic pediatric patients 3 years of age and older with late infantile neuronal ceroid lipofuscinosis type 2 (CLN2), also known as tripeptidyl peptidase 1 (TPP1) deficiency.

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review: tripeptidyl peptidase 1 (TPP1) enzyme assay or genetic testing results supporting diagnosis.

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a neurologist.

IV. CRITERIA FOR APPROVAL

Late infantile neuronal ceroid lipofuscinosis type 2 (CLN2)

Authorization of 12 months may be granted for members with CLN2 when ALL of the following criteria are met:
1. Diagnosis of CLN2 was confirmed by enzyme assay demonstrating a deficiency of tripeptidyl peptidase 1 (TPP1) enzyme activity or by genetic testing.
2. Brineura is prescribed to slow the loss of ambulation in symptomatic members
3. Member is 3 years of age or older
4. Brineura will be administered by, or under the direction of a physician knowledgeable in intraventricular administration
5. Dosage of Brineura will not exceed 300 mg once every other week

V. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.
VI. REFERENCES

QUANTITY LIMIT CRITERIA

**BRAND NAME**
(generic)
(buprenorphine sublingual tablets)

**Status:** CVS Caremark Criteria
**Type:** Quantity Limit

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

**FDA-APPROVED INDICATIONS**
Buprenorphine sublingual tablets are indicated for the treatment of opioid dependence and are preferred for induction. Buprenorphine sublingual tablets should be used as part of a complete treatment plan to include counseling and psychosocial support.

**RATIONALE**
Buprenorphine sublingual tablets are indicated for the treatment of opioid dependence and are preferred for induction. Buprenorphine sublingual tablets should be used as part of a complete treatment plan to include counseling and psychosocial support.1-3

If using buprenorphine for induction, consideration should be given to the type of opioid dependence (i.e., long- or short-acting opioid products) the time since last opioid use, and the degree or level of opioid dependence. It is recommended that an adequate treatment dose, titrated to clinical effectiveness, should be achieved as rapidly as possible. The dosing on the initial day of treatment may be given in 2 mg to 4 mg increments if preferred.1-3

Buprenorphine/naloxone sublingual tablets are preferred for maintenance treatment. However, buprenorphine sublingual tablets may be used for maintenance in patients who cannot tolerate the presence of naloxone.1-3 Buprenorphine sublingual tablets are a reasonable and recommended alternative to methadone for pregnant and/or breastfeeding women.4 After treatment induction and stabilization, the maintenance dose of buprenorphine sublingual tablets is generally in the range of 4 mg to 24 mg buprenorphine per day depending on the individual patient. The recommended target dosage of buprenorphine sublingual tablets is 16 mg as a single daily dose. Dosages higher than 24 mg have not been demonstrated to provide any clinical advantage. There is no maximum recommended duration of maintenance treatment. Patients may require treatment indefinitely and should continue for as long as patients are benefiting and the use of buprenorphine sublingual tablets contributes to the intended treatment goals.1-3 The quantity limit will allow 90 buprenorphine sublingual tablets per month to allow for a maximum of 24 mg per day at the highest available strength.

If the patient is requesting more than the initial quantity limit, then the claim will reject with a message indicating that quantity limits are exceeded.

**REFERENCES**
**LIMIT CRITERIA**

Limits do not accumulate together. Patient is allowed the maximum limit for each drug and strength.

<table>
<thead>
<tr>
<th>Drug</th>
<th>1 Month Limit*</th>
<th>3 Month Limit*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine SL tab 2 mg</td>
<td>90 units / 25 days</td>
<td>270 units / 75 days</td>
</tr>
<tr>
<td>Buprenorphine SL tab 8 mg</td>
<td>90 units / 25 days</td>
<td>270 units / 75 days</td>
</tr>
</tbody>
</table>

*The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*
QUANTITY LIMIT CRITERIA

<table>
<thead>
<tr>
<th>BRAND NAME* (generic)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUNAVAIL (buprenorphine and naloxone buccal film)</td>
</tr>
<tr>
<td>CASSIPA (buprenorphine and naloxone sublingual film)</td>
</tr>
<tr>
<td>SUBOXONE (buprenorphine and naloxone sublingual tablet and film)</td>
</tr>
<tr>
<td>ZUBSOLV (buprenorphine and naloxone sublingual tablet)</td>
</tr>
</tbody>
</table>

Status: CVS Caremark Criteria
Type: Quantity Limit
Ref # 1553-H

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Bunavail
Bunavail is indicated for the treatment of opioid dependence. Bunavail should be used as part of a complete treatment plan that includes counseling and psychosocial support.

Cassipa
Cassipa is indicated for the maintenance treatment of opioid dependence. Cassipa should be used as part of a complete treatment plan to include counseling and psychosocial support.

Suboxone Film
Suboxone sublingual film is indicated for treatment of opioid dependence. Suboxone sublingual film should be used as part of a complete treatment plan that includes counseling and psychosocial support.

Suboxone Tablet
Buprenorphine and Naloxone sublingual tablets are indicated for the maintenance treatment of opioid dependence. Buprenorphine and Naloxone sublingual tablets should be used as part of a complete treatment plan that includes counseling and psychosocial support.

Zubsolv
Zubsolv is indicated for treatment of opioid dependence. Zubsolv should be used as part of a complete treatment plan that includes counseling and psychosocial support.

RATIONALE

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Bunavail (buprenorphine/naloxone buccal film), Cassipa (buprenorphine/naloxone sublingual film), Suboxone (buprenorphine/naloxone sublingual tablet and film), and Zubsolv (buprenorphine/naloxone sublingual tablet) are indicated for the treatment of opioid dependence and should be used as part of a complete treatment plan that includes counseling and psychosocial support.1-7

If using buprenorphine/naloxone for induction, consideration should be given to the type of opioid dependence (i.e., long- or short-acting opioid products), the time since last opioid use, and the degree or level of opioid dependence. The maintenance dose of Suboxone is generally in the range of 4 mg/1 mg buprenorphine/naloxone to 24 mg/6 mg buprenorphine/naloxone per day depending on the individual and clinical response. The recommended target dosage of Suboxone during maintenance is 16 mg/4mg buprenorphine/naloxone per day as a single daily dose. Dosages higher than 24 mg/6 mg buprenorphine/naloxone daily have not been demonstrated to provide a clinical advantage. The maintenance dose of Bunavail is generally in the range of 2.1 mg/0.3 mg to 12.6 mg/2.1 mg per day depending on the individual patient and clinical response. The recommended target dosage of Bunavail buccal film during maintenance is 8.4 mg/1.4 mg buprenorphine/naloxone per day as a single daily dose. Dosages higher than 12.6 mg/2.1 mg have not been demonstrated to provide any clinical advantage. The maintenance dose of Zubsolv is generally in the range of 2.9 mg/0.71 mg buprenorphine/naloxone to 17.2 mg/4.2 mg buprenorphine/naloxone per day depending on the individual patient and clinical response. The recommended target dosage of Zubsolv during maintenance is 11.4 mg/2.9 mg buprenorphine/naloxone as a single daily dose. Dosages higher than 17.2 mg/4.2 mg buprenorphine/naloxone have not been demonstrated to provide any clinical advantage. Cassipa (16 mg/4 mg) should only be used after induction and stabilization of the patient, and when the patient has been titrated to a dose of 16 mg of buprenorphine using another marketed product. The dosage of buprenorphine and naloxone sublingual film may need to be adjusted to a level that holds the patient in treatment and suppresses opioid withdrawal signs and symptoms. Cassipa comes in a single dose and cannot be adjusted.1-7

If the patient is requesting more than the initial quantity limit, then the claim will reject with a message indicating that quantity limits are exceeded.

REFERENCES

Written by:  UM Development (CF/JH)
Date Written:  11/2016
Revised:  (CF/JH) 01/2017 (no clinical changes), 11/2017 (no clinical changes); (DS) 09/2018 (added Cassipa); (CF) 11/2018 (no clinical changes)
Reviewed:  Medical Affairs: (DNC) 11/2016, 10/2018
External Review:  12/2016, 04/2017, 02/2018, 10/2018, 02/2019
**LIMIT CRITERIA**

Limits do not accumulate together. Patient is allowed the maximum limit for each drug and strength.

<table>
<thead>
<tr>
<th>Drug</th>
<th>1 Month Limit*</th>
<th>3 Month Limit*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bunavail 2.1 mg/0.3 mg, 4.2 mg/0.7 mg</td>
<td>90 units / 25 days</td>
<td>270 units / 75 days</td>
</tr>
<tr>
<td>Bunavail 6.3 mg/1 mg</td>
<td>60 units / 25 days</td>
<td>180 units / 75 days</td>
</tr>
<tr>
<td>Cassipa 16 mg/4 mg</td>
<td>30 units / 25 days</td>
<td>90 units / 75 days</td>
</tr>
<tr>
<td>Suboxone 2 mg/0.5 mg, 4 mg/1 mg, 8 mg/2 mg</td>
<td>90 units / 25 days</td>
<td>270 units / 75 days</td>
</tr>
<tr>
<td>Suboxone 12 mg/3 mg</td>
<td>60 units / 25 days</td>
<td>180 units / 75 days</td>
</tr>
<tr>
<td>Zubsov 0.7 mg/0.18 mg, 1.4 mg/0.36 mg, 2.9 mg/0.71 mg, 5.7 mg/1.4 mg</td>
<td>90 units / 25 days</td>
<td>270 units / 75 days</td>
</tr>
<tr>
<td>Zubsov 8.6 mg/2.1 mg</td>
<td>60 units / 25 days</td>
<td>180 units / 75 days</td>
</tr>
<tr>
<td>Zubsov 11.4 mg/2.9 mg</td>
<td>30 units / 25 days</td>
<td>90 units / 75 days</td>
</tr>
</tbody>
</table>

*The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*
QUANTITY LIMIT CRITERIA

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>BUTALBITAL CONTAINING ANALGESICS (BRAND AND GENERIC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRAND NAME*</td>
<td>(generic)</td>
</tr>
<tr>
<td></td>
<td>(butalbital and acetaminophen)</td>
</tr>
<tr>
<td></td>
<td>(butalbital, acetaminophen, and caffeine)</td>
</tr>
<tr>
<td></td>
<td>(butalbital, acetaminophen, caffeine, and codeine)</td>
</tr>
<tr>
<td></td>
<td>(butalbital, aspirin, and caffeine)</td>
</tr>
<tr>
<td></td>
<td>(butalbital, aspirin, caffeine, and codeine)</td>
</tr>
</tbody>
</table>

Status: CVS Caremark Criteria
Type: Quantity Limit
Ref # 38-H

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS
Butalbital containing products are indicated for the relief of the symptom complex of tension (or muscle contraction) headache.

Evidence supporting the efficacy and safety of these combination products in the treatment of multiple recurrent headaches is unavailable. Caution in this regard is required because butalbital is habit-forming and potentially abusable.

RATIONALE
Butalbital containing products are indicated for the relief of the symptom complex of tension (or muscle contraction) headache. Evidence supporting the efficacy and safety of these combination products in the treatment of multiple recurrent headaches is unavailable. Caution in this regard is required because butalbital is habit-forming and potentially abusable.1-10

Drug treatment of acute headache should generally not exceed more than two days per week on a regular basis. More frequent treatment other than this may result in medication-overuse chronic daily headaches.11

The recommended dosage of butalbital 25 mg and acetaminophen 325 mg tablets is two tablets every four hours. The total daily dose should not exceed 12 tablets. The recommended dosage of all other butalbital combination products is one or two tablets/capsules/teaspoonfuls every four hours as needed. The total daily dose should not exceed 6 tablets/capsules/teaspoonfuls. Extended and repeated use of these products is not recommended because of the potential for physical dependence.1-10

Butalbital Products Limit 38-H 06-2019
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The limit is set to 6 doses per day at the maximum daily dose for acute treatment of 8 headaches per month. If the patient is requesting more than the initial quantity limit, then the claim will reject with a message indicating that quantity limits are exceeded.

REFERENCES

LIMIT CRITERIA
This quantity limit should accumulate across all drugs and strengths up to highest quantity listed depending on the order the claims are processed.

<table>
<thead>
<tr>
<th>Drug</th>
<th>1 Month Limit*</th>
<th>3 Month Limit*</th>
</tr>
</thead>
<tbody>
<tr>
<td>butalbital, acetaminophen, and caffeine syrup</td>
<td>720 mL / 25 days</td>
<td>2160 mL / 75 days</td>
</tr>
<tr>
<td>butalbital 25 mg and acetaminophen 325 mg</td>
<td>96 units / 25 days</td>
<td>288 units / 75 days</td>
</tr>
<tr>
<td>butalbital and acetaminophen</td>
<td>48 units / 25 days</td>
<td>144 units / 75 days</td>
</tr>
<tr>
<td>butalbital, acetaminophen, and caffeine</td>
<td>48 units / 25 days</td>
<td>144 units / 75 days</td>
</tr>
<tr>
<td>butalbital, acetaminophen, caffeine, and codeine</td>
<td>48 units / 25 days</td>
<td>144 units / 75 days</td>
</tr>
<tr>
<td>butalbital, aspirin, and caffeine</td>
<td>48 units / 25 days</td>
<td>144 units / 75 days</td>
</tr>
<tr>
<td>butalbital, aspirin, caffeine, and codeine</td>
<td>48 units / 25 days</td>
<td>144 units / 75 days</td>
</tr>
</tbody>
</table>

*The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing. The limit criteria apply to both brand and generic, if available.*
QUANTITY LIMIT CRITERIA

<table>
<thead>
<tr>
<th>BRAND NAME*</th>
</tr>
</thead>
<tbody>
<tr>
<td>(generic)</td>
</tr>
<tr>
<td><em>butorphanol tartrate nasal spray</em></td>
</tr>
</tbody>
</table>

**Status:** CVS Caremark Criteria  
**Type:** Quantity Limit  
Ref # 212-H

*Drugs that are listed in the target drug box include both brand and generic and all dosages forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

**FDA-APPROVED INDICATIONS**

Butorphanol tartrate nasal spray is indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

**Limitations of Use**

Because of the risks of addiction, abuse, and misuse, with opioids, even at recommended doses, reserve butorphanol tartrate nasal spray for use in patients for whom alternative treatment options [e.g., non-opioid analgesics] have not been tolerated, or are not expected to be tolerated, or have not provided adequate analgesia, or are not expected to provide adequate analgesia.

**RATIONALE**

Butorphanol tartrate nasal spray is indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. Because of the risks of addiction, abuse, and misuse, with opioids, even at recommended doses, reserve butorphanol tartrate nasal spray for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]: have not been tolerated, or are not expected to be tolerated; or, have not provided adequate analgesia, or are not expected to provide adequate analgesia.

In clinical trials, butorphanol was evaluated for several types of pain, including postoperative pain and migraine headache pain. Some experts state that butorphanol tartrate nasal spray may be considered when other antimigraine drugs cannot be used or as rescue therapy when sedative effects will not place the patient at risk. Butorphanol tartrate, by all routes of administration, has been associated with episodes of abuse. Of the cases received, there were more reports of abuse with the nasal spray formulation than with the injectable formulation. Proper assessment of the patient, proper prescribing practices, periodic re-evaluation of therapy, and proper dispensing and storage are appropriate measures that help to limit abuse of opioid drugs. Strategies to reduce these risks include prescribing the drug in the smallest appropriate quantity and advising the patient on the proper disposal of unused drug.

The usual recommended dose for initial nasal administration of butorphanol tartrate nasal solution is 1 mg (1 spray in one nostril). If adequate pain relief is not achieved within 60 to 90 minutes, an additional 1 mg dose may be given. Depending on the severity of the pain, an initial dose of 2 mg (1 spray in each nostril) may be used in patients who will be able to remain recumbent in the event drowsiness or dizziness occurs. In such patients, single additional 2 mg doses should not be given for 3 to 4 hours. Individually titrate butorphanol tartrate nasal spray to a dose that provides adequate analgesia and minimizes adverse reactions.

The initial limit criteria are intended to meet the immediate need of a patient being discharged from the hospital with postoperative pain or of a migraine patient in acute need of rescue therapy.
Butorphanol Tartrate Nasal Spray 10 mg/mL is supplied in a 2.5 mL bottle of nasal spray solution with a metered-dose spray pump. On average, one bottle will deliver 14 to 15 doses if no repriming is necessary.1-3 The initial quantity limit is set at 2 bottles (28-30 doses) per month to allow for up to 5 days of treatment for post-operative pain or for approximately 4 migraine headaches per month.

If the patient is requesting more than the initial quantity limit, then the claim will reject with a message indicating that a prior authorization is required.

REFERENCES

LIMIT CRITERIA

<table>
<thead>
<tr>
<th>Drug</th>
<th>1 Month Limit*</th>
<th>3 Month Limit*</th>
</tr>
</thead>
<tbody>
<tr>
<td>butorphanol nasal spray</td>
<td>2 bottles / 25 days</td>
<td>6 bottles / 75 days</td>
</tr>
</tbody>
</table>

*The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.
PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>BRAND NAME*</th>
</tr>
</thead>
<tbody>
<tr>
<td>(generic)</td>
</tr>
</tbody>
</table>

(butorphanol tartrate nasal spray)

**Status:** CVS Caremark Criteria

**Type:** Post Limit Prior Authorization

*Drugs that are listed in the target drug box include both brand and generic and all dosages forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

**FDA-APPROVED INDICATIONS**

Butorphanol tartrate nasal spray is indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

**Limitations of Use**

- Have not been tolerated, or are not expected to be tolerated,
- Have not provided adequate analgesia, or are not expected to provide adequate analgesia

**COVERAGE CRITERIA**

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has a diagnosis of migraine headache
- Medication overuse headache has been ruled out
- The patient is unable to take abortive migraine therapy due to an inadequate treatment response, intolerance, or contraindication [Note: Examples of abortive therapy are triptans, ergotamine, dihydroergotamine, nonsteroidal anti-inflammatory drugs (NSAIDs), mixed analgesics containing caffeine, isomethetene, or butalbital.]
- The patient is currently using migraine prophylactic therapy or unable to take migraine prophylactic therapies due to an inadequate treatment response, intolerance, or contraindication [Note: Examples of prophylactic therapy are divalproex sodium, topiramate, valproate sodium, metoprolol, propranolol, timolol, atenolol, nadolol, amitriptyline, venlafaxine.]

**RATIONALE**

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Butorphanol tartrate nasal spray is indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. Because of the risks of addiction, abuse, and misuse, with opioids, even at recommended doses, reserve butorphanol tartrate nasal spray for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]:

Butorphanol Nasal Solution (Stadol) Post Limit 213-J 06-2019

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have not been tolerated, or are not expected to be tolerated; or, have not provided adequate analgesia, or are not expected to provide adequate analgesia.\textsuperscript{1-3}

In clinical trials, butorphanol was evaluated for several types of pain, including postoperative pain, and migraine headache pain.\textsuperscript{1-3} The American Headache Society considers specific medications within the following classes effective for the acute therapy of migraine: analgesics, ergots, nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, triptans, and certain combination medications. Isometheptene is considered probably effective, and butalbital combination products are considered possibly effective.\textsuperscript{6} Some experts state that butorphanol tartrate nasal spray may be considered when other antimigraine drugs cannot be used or as rescue therapy when sedative effects will not place the patient at risk.\textsuperscript{1-3} The Institute for Clinical Systems Improvement (ICSI) Diagnosis and Treatment of Headache guideline does not recommend the use of butorphanol because of its high potential for abuse and adverse side-effect profile.\textsuperscript{9} Butorphanol tartrate, by all routes of administration, has been associated with episodes of abuse. Of the cases received, there were more reports of abuse with the nasal spray formulation than with the injectable formulation. Proper assessment of the patient, proper prescribing practices, periodic re-evaluation of therapy, and proper dispensing and storage are appropriate measures that help to limit abuse of opioid drugs. Strategies to reduce these risks include prescribing the drug in the smallest appropriate quantity and advising the patient on the proper disposal of unused drug.\textsuperscript{1-3} Therefore, patients with migraine headache must be unable to take other abortive migraine therapy due to an inadequate response, intolerance, or contraindication. The patient must also have experienced an inadequate treatment response, intolerance, or contraindication to at least two oral opioids (or is unable to take oral medications including liquids) prior to butorphanol nasal spray.

For prevention of migraine headache, the American Academy of Neurology and the American Headache Society 2012 guideline update recommendations state that the following medications are established as effective and should be offered for migraine prevention: antiepileptic drugs (divalproex sodium, sodium valproate, topiramate); \(\beta\)-blockers (metoprolol, propranolol, timolol); triptans (frovatriptan) for short-term prophylaxis of menstrually related migraines (MRMs). Additionally, the following medications are probably effective and should be considered for migraine prevention: antidepressants (amitriptyline, venlafaxine); \(\beta\)-blockers (atenolol, nadolol); triptans (naratriptan, zolmitriptan) for short-term prophylaxis of menstrually related migraines (MRMs).\textsuperscript{5} The choice of prophylactic agent depends upon side effect profile, comorbid conditions, medication interactions, evidence-based efficacy, and patient preference.\textsuperscript{4} Therefore, patients with migraine headache must be currently using migraine prophylactic therapy or unable to take migraine prophylactic therapies due to inadequate treatment response, intolerance, or contraindication.

Drug treatment of acute headache should generally not exceed more than two days per week on a regular basis. More frequent treatment other than this may result in medication-overuse chronic daily headaches.\textsuperscript{4} Therefore, the prescriber must have considered and ruled out the diagnosis of medication overuse headache.

The usual recommended dose for initial nasal administration of butorphanol tartrate nasal solution is 1 mg (1 spray in one nostril). If adequate pain relief is not achieved within 60 to 90 minutes, an additional 1 mg dose may be given. Depending on the severity of the pain, an initial dose of 2 mg (1 spray in each nostril) may be used in patients who will be able to remain recumbent in the event drowsiness or dizziness occurs. In such patients, single additional 2 mg doses should not be given for 3 to 4 hours. Individually titrate butorphanol tartrate nasal spray to a dose that provides adequate analgesia and minimizes adverse reactions.\textsuperscript{1-3}

Butorphanol Tartrate Nasal Spray 10 mg/mL is supplied in a 2.5 mL bottle of nasal spray solution with a metered-dose spray pump. On average, one bottle will deliver 14 to 15 doses if no repriming is necessary.\textsuperscript{1-3} The post quantity limits are set at a quantity sufficient to treat 8 headaches per month.

Additional quantities for non-migraine pain are not available in this post limit document.

REFERENCES
<table>
<thead>
<tr>
<th>CRITERIA FOR APPROVAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Does the patient have a diagnosis of migraine headache?</td>
</tr>
<tr>
<td>2. Has medication overuse headache been ruled out?</td>
</tr>
<tr>
<td>3. Is the patient unable to take abortive migraine therapy due to an inadequate treatment response, intolerance, or contraindication?</td>
</tr>
<tr>
<td>[Note: Examples of abortive therapy are triptans, ergotamine, dihydroergotamine, nonsteroidal anti-inflammatory drugs (NSAIDs), mixed analgesics containing caffeine, isometheptene, or butalbital.]</td>
</tr>
<tr>
<td>4. Is the patient currently using migraine prophylactic therapy or unable to take migraine prophylactic therapies due to an inadequate treatment response, intolerance, or contraindication?</td>
</tr>
<tr>
<td>[Note: Examples of prophylactic therapy are divalproex sodium, topiramate, valproate sodium, metoprolol, propranolol, timolol, atenolol, nadolol, amitriptyline, venlafaxine.]</td>
</tr>
<tr>
<td>5. Has the patient experienced an inadequate treatment response, intolerance, or contraindication to at least two oral opioids?</td>
</tr>
<tr>
<td>[If yes, then skip to question 7.]</td>
</tr>
<tr>
<td>6. Is the patient unable to take oral medications, including liquids?</td>
</tr>
<tr>
<td>7. Does the patient require MORE than the plan allowance of 4 bottles per month?</td>
</tr>
<tr>
<td>[RPh Note: If yes, then deny and enter a partial approval for 4 bottles per 25 days or 12 bottles per 75 days.]</td>
</tr>
<tr>
<td>No.</td>
</tr>
<tr>
<td>-----</td>
</tr>
</tbody>
</table>
| 1.  | Go to 2     | Deny        | You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when you have migraine headaches. Your request has been denied based on the information we have.  
[Short Description: No approvable diagnosis.] |
| 2.  | Go to 3     | Deny        | You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when a headache from overuse of migraine medication has been considered and ruled out. Your request has been denied based on the information we have.  
[Short Description: Medication overuse headache not ruled out.] |
| 3.  | Go to 4     | Deny        | You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when you have tried medicine to help treat a migraine and it either did not work for you or you cannot take it. Your request has been denied based on the information we have.  
[Short Description: No trial of abortive migraine therapy.] |
| 4.  | Go to 5     | Deny        | You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when you meet one of these conditions:  
- You currently take medicine to help prevent migraines  
- You have tried medicine to help prevent a migraine and it either did not work for you or you cannot take it  
Your request has been denied based on the information we have.  
[Short Description: No trial of prophylactic migraine therapy.] |
| 5.  | Go to 7     | Go to 6    | Deny        | You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when you meet one of these conditions:  
- You have tried two oral opioids and they either did not work for you or you cannot take them  
- You are unable to take oral medications, including liquids  
Your request has been denied based on the information we have.  
[Short Description: Patient is able to take oral meds but has not tried 2 oral opioids.] |
| 6.  | Go to 7     | Deny        | You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when you meet one of these conditions:  
- You have tried two oral opioids and they either did not work for you or you cannot take them  
- You are unable to take oral medications, including liquids  
Your request has been denied based on the information we have.  
[Short Description: Patient is able to take oral meds but has not tried 2 oral opioids.] |

### Short Descriptions: 
- Over max quantity.
SPECIALTY GUIDELINE MANAGEMENT

CABLIVI (caplacizumab-yhdp)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Cablivi is indicated for the treatment of adult patients with acquired thrombotic thrombocytopenic purpura (aTTP), in combination with plasma exchange and immunosuppressive therapy.

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

For continuation of therapy: medical record documentation of signs of persistent underlying aTTP

III. CRITERIA FOR INITIAL APPROVAL

Acquired thrombotic thrombocytopenic purpura (aTTP)
Authorization of 30 days may be granted for treatment of acquired thrombotic thrombocytopenic purpura (aTTP) after the plasma exchange period in the inpatient setting when all of the following criteria are met:
A. The member received the requested medication with plasma exchange.
B. The requested medication will be given in combination with immunosuppressive therapy.
C. The member will not receive the requested medication beyond 30 days from the cessation of plasma exchange unless the member has documented persistent aTTP.
D. The member has not received more than 2 distinct courses of therapy with the requested medication. (Distinct courses include treatment for recurrences during or after treatment with the requested medication. A recurrence is when the patient needs to reinitiate plasma exchange. A 28 day extension of therapy does not count as a recurrence.)

IV. CONTINUATION OF THERAPY

Authorization of 28 days may be granted for continuation of therapy for aTTP when all of the following criteria are met:
A. The request for continuation of therapy is for extension of therapy after the initial course of the requested medication (initial course: treatment with the requested medication during and 30 days after plasma exchange).
B. The member has either of the following documented signs of persistent underlying aTTP:
   1. ADAMTS13 activity level less than 10% or
2. All of the following:
   a. Microangiopathic hemolytic anemia (MAHA) documented by the presence of schistocytes on peripheral smear
   b. Thrombocytopenia (platelet count below normal per laboratory reference range), and
   c. Elevated lactate dehydrogenase (LDH) level (LDH level above normal per laboratory reference range)

C. The member has not received a prior 28 day extension of therapy after the initial course of the requested medication for this course of treatment.
D. The member has not received more than 2 distinct courses of therapy with the requested medication. (Distinct courses include treatment for recurrences during or after treatment with the requested medication. A recurrence is when the patient needs to reinitiate plasma exchange. A 28 day extension of therapy does not count as a recurrence.)

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

CABOMETYX (cabozantinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
   Cabometyx is indicated for the treatment of patients with:
   1. Advanced renal cell carcinoma (RCC)
   2. Hepatocellular carcinoma (HCC) who have been previously treated with sorafenib

B. Compendial Uses
   1. Relapsed or surgically unresectable stage IV kidney cancer
   2. Non-small cell lung cancer
   3. Hepatocellular carcinoma (HCC) who have been previously treated with lenvatinib

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of RET gene rearrangement documentation is necessary to initiate the prior authorization review for the indication of non-small cell lung cancer.

III. CRITERIA FOR INITIAL APPROVAL

A. Renal Cell Carcinoma
   Authorization of 12 months may be granted for treatment of relapsed, unresectable, or metastatic renal cell carcinoma.

B. Hepatocellular carcinoma (HCC)
   Authorization of 12 months may be granted for treatment of hepatocellular carcinoma (HCC) who have been previously treated with sorafenib (Nexavar) or lenvatinib (Lenvima).

C. Non-small Cell Lung Cancer
   Authorization of 12 months may be granted for treatment of RET (rearranged during transfection) positive non-small cell lung cancer.

IV. CONTINUATION OF THERAPY
Authorization of 12 months may be granted for continuation of therapy for an indication outlined in Section III when there is no evidence of unacceptable toxicity or disease progression on the current regimen.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

CALQUENCE (acalabrutinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
   Calquence is indicated for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy.

B. Compendial Use
   Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL), relapsed or refractory

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: For ibrutinib-refractory CLL/SLL, BTK C481S mutation status

III. CRITERIA FOR INITIAL APPROVAL

A. Mantle cell lymphoma
   Authorization of 12 months may be granted for treatment of mantle cell lymphoma when the member has received at least one prior therapy.

B. Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL)
   Authorization of 12 months may be granted for treatment of relapsed or refractory CLL/SLL when the member does not have ibrutinib (Imbruvica)-refractory disease with BTK C481S mutation.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

CAPRELSA (vandetanib)

POLICY

I. INDICATIONS
The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Treatment of symptomatic or progressive medullary thyroid cancer in patients with unresectable locally advanced or metastatic disease

*Use Caprelsa in patients with indolent, asymptomatic or slowly progressing disease only after careful consideration of the treatment related risks of Caprelsa.*

B. Compendial Uses
1. Follicular, Hurthle cell, and papillary thyroid carcinoma
2. Non-small cell lung cancer with RET gene rearrangements

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION
Submission of RET gene rearrangement documentation is necessary to initiate the prior authorization review for the indication of non-small cell lung cancer.

III. CRITERIA FOR INITIAL APPROVAL

A. Thyroid carcinoma (follicular, Hürthle cell, papillary)
Authorization of 12 months may be granted for the treatment of radioiodine refractory follicular, Hürthle cell, or papillary thyroid carcinoma.

B. Medullary thyroid carcinoma
Authorization of 12 months may be granted for the treatment of medullary thyroid carcinoma.

C. Non-small cell lung cancer (NSCLC)
Authorization of 12 months may be granted for the treatment of NSCLC with RET gene rearrangements.

IV. CONTINUATION OF THERAPY
Authorization of 12 months may be granted for continuation of therapy for an indication outlined in Section III when there is no evidence of unacceptable toxicity or disease progression on the current regimen.

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

CARBAGLU (carglumic acid)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Acute hyperammonemia in patients with NAGS deficiency
      Carbaglu is indicated as an adjunctive therapy in pediatric and adult patients for the treatment of acute hyperammonemia due to the deficiency of the hepatic enzyme N-acetylglutamate synthase (NAGS). During acute hyperammonemic episodes, concomitant administration of Carbaglu with other ammonia lowering therapies such as alternate pathway medications, hemodialysis, and dietary protein restriction is recommended.

   2. Maintenance therapy for chronic hyperammonemia in patients with NAGS deficiency
      Carbaglu is indicated for maintenance therapy in pediatric and adult patients for chronic hyperammonemia due to the deficiency of the hepatic enzyme NAGS. During maintenance therapy, the concomitant use of other ammonia lowering therapies and protein restriction may be needed based on plasma ammonia levels.

B. Compendial Uses
   1. Methylmalonic acidemia
   2. Propionic acidemia

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. N-acetylglutamate synthase (NAGS) Deficiency
   Authorization of indefinite approval may be granted for members with diagnosis of NAGS deficiency confirmed by enzymatic or genetic testing.

B. Methylmalonic Acidemia
   Authorization of indefinite approval may be granted for members who have a diagnosis of methylmalonic acidemia.

C. Propionic Acidemia
   Authorization of indefinite approval may be granted for members who have a diagnosis of propionic acidemia.

III. CONTINUATION OF THERAPY
All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

CAYSTON (aztreonam for inhalation solution)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Cayston is indicated to improve respiratory symptoms in cystic fibrosis patients with Pseudomonas aeruginosa.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Cystic Fibrosis
Authorization of 24 months may be granted for members with cystic fibrosis when Pseudomonas aeruginosa is present in airway cultures OR the member has a history of Pseudomonas aeruginosa infection or colonization in the airways.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

CERDELGA (eliglustat)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Cerdelga is indicated for the long-term treatment of adult patients with Gaucher disease type 1 who are CYP2D6 extensive metabolizers, intermediate metabolizers, or poor metabolizers as detected by an FDA-cleared test.

Limitations of use: Patients who are CYP2D6 ultra-rapid metabolizers may not achieve adequate concentrations of Cerdelga to achieve a therapeutic effect. A specific dosage cannot be recommended for those patients whose CYP2D6 genotype cannot be determined (indeterminate metabolizers).

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Gaucher disease type 1
Authorization of 24 months may be granted for treatment of Gaucher disease type 1 when all of the following criteria are met:
1. Diagnosis of Gaucher disease was confirmed by enzyme assay demonstrating a deficiency of beta-glucocerebrosidase (glucosidase) enzyme activity or by genetic testing
2. Member is a CYP2D6 extensive metabolizer, an intermediate metabolizer, or a poor metabolizer as detected by an FDA-cleared test

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

CEREZYME (imiglucerase)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Cerezyme is indicated for long-term enzyme replacement therapy (ERT) for pediatric and adult patients with a confirmed diagnosis of type 1 Gaucher disease that results in one or more of the following conditions: anemia, thrombocytopenia, bone disease, hepatomegaly, or splenomegaly.

B. Compendial Uses

Gaucher disease type 3

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Gaucher disease type 1

Indefinite authorization may be granted for treatment of Gaucher disease type 1 when the diagnosis of Gaucher disease was confirmed by enzyme assay demonstrating a deficiency of beta-glucocerebrosidase (glucosidase) enzyme activity or by genetic testing.

B. Gaucher disease type 3

Indefinite authorization may be granted for treatment of Gaucher disease type 3 when the diagnosis of Gaucher disease was confirmed by enzyme assay demonstrating a deficiency of beta-glucocerebrosidase (glucosidase) enzyme activity or by genetic testing.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

CETROTIDE (cetrorelix acetate)
ganirelix acetate

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Cetrotide and ganirelix are indicated for the inhibition of premature luteinizing hormone (LH) surges in women undergoing controlled ovarian stimulation.

All other indications are considered experimental/investigational and are not a covered benefit.

II. MEDICAL BENEFIT ALIGNMENT

Specialty Guideline Management coverage review will be bypassed for drug(s) being requested for a procedure that has been approved under a member’s medical benefit plan. Such members will be exempt from the requirements in Sections III and IV. A medical authorization number and confirmation of the approved procedure(s) will be required.

NOTE: Some plans may opt-out of medical benefit alignment. Members receiving coverage under such plans must meet the requirements in Sections III and IV.

III. CRITERIA FOR INITIAL APPROVAL

Inhibition of premature LH surges
Authorization of 12 months may be granted for the inhibition of premature LH surges in members undergoing ovulation induction or assisted reproductive technology (ART).

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

## PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>CALCITONIN GENE-RELATED PEPTIDE (CGRP) RECEPTOR ANTAGONISTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRAND NAME* (generic)</td>
<td></td>
</tr>
<tr>
<td>AIMOVIG (erenumab-aooe injection)</td>
<td></td>
</tr>
<tr>
<td>AJOVY (fremanezumab-vfrm injection)</td>
<td></td>
</tr>
<tr>
<td>EMGALITY (galcanezumab-gnIm injection)</td>
<td></td>
</tr>
</tbody>
</table>

**Status:** CVS Caremark Criteria  
**Ref #** 2581-C  
**Type:** Initial Prior Authorization  
**Ref #** REG 3160-C

*Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

### FDA-APPROVED INDICATIONS

**Aimovig**  
Aimovig is indicated for the preventive treatment of migraine in adults.

**Ajovy**  
Ajovy is indicated for the preventive treatment of migraine in adults.

**Emgality**  
- **Migraine**  
  Emgality is indicated for the preventive treatment of migraine in adults  
  - **Cluster Headache**  
    Emgality is indicated for the treatment of episodic cluster headaches in adults

### COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the preventive treatment of migraine in an adult patient  
  AND  
  - The patient received at least 3 months of treatment with the requested drug and had a reduction in migraine days per month from baseline  
    OR  
    - The patient experienced an inadequate treatment response with an 8-week trial of any of the following: Antiepileptic drugs (AEDs) (e.g., divalproex sodium, topiramate, valproate sodium), Beta-adrenergic blocking agents (e.g., metoprolol, propranolol, timolol, atenolol, nadolol), Antidepressants (e.g., amitriptyline, venlafaxine)  
      OR  
      - The patient experienced an intolerance or has a contraindication that would prohibit an 8-week trial of any of the following: Antiepileptic drugs (AEDs) (e.g., divalproex sodium, topiramate, valproate sodium), Beta-adrenergic blocking agents (e.g., metoprolol, propranolol, timolol, atenolol, nadolol), Antidepressants (e.g., amitriptyline, venlafaxine)  
    OR  
    - The request is for Emgality 100mg for treatment of episodic cluster headaches in adults  
      AND
- The patient received at least 3 weeks treatment with the requested drug and had a reduction in weekly cluster headache attack frequency from baseline
  **OR**
- The patient experienced an inadequate treatment response with sumatriptan (subcutaneous or nasal) or zolmitriptan (nasal or oral)
  **OR**
- The patient experienced an intolerance or contraindication to sumatriptan (subcutaneous or nasal) or zolmitriptan (nasal or oral)

Quantity limits apply.

**RATIONALE**

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Aimovig, Ajovy, and Emgality are indicated for the preventive treatment of migraine in adults. Emgality is also indicated for the treatment of episodic cluster headaches in adults.

In the Aimovig clinical study, a protocol amendment that was implemented during the enrollment period allowed the enrollment of patients with concomitant use of one migraine-preventive medication taken at a stable dose (i.e., with no changes to the dose within 2 months before the baseline phase or at any time during the trial). In the Ajovy clinical study, a subset of patients was allowed to use one additional concomitant preventive medication. In the Emgality clinical study, a subset of patients was allowed to use one concomitant migraine preventive medication.

For prevention of migraine headache, the American Academy of Neurology (AAN) and the American Headache Society (AHS) 2012 guideline update recommendations state that the following medications are established as effective and should be offered for migraine prevention: β-adrenergic blocking agents, metoprolol, propranolol, timolol; and antiepileptic drugs (AEDs), divalproex sodium, topiramate, sodium valproate. Additionally, the following medications are probably effective: antidepressants, amitriptyline, venlafaxine; and β-adrenergic blocking agents, atenolol, nadolol, and should be considered for migraine prevention. Although triptans are recommended by the AAN and AHS guideline, these medications were not included as a criteria trial option because recommended use was for short-term prophylaxis of menstruation-associated migraine (MAM). Calcium channel blockers (CCBs) are not included as a criteria trial option based on the AAN and AHS guideline which categorizes nicardipine as possibly effective and nifedipine, nimodipine, verapamil as having inadequate or conflicting data to support or refute medication use. Therefore, the trial drug criteria options will include the drug classes the AAN and AHS guideline recommended as effective and should be offered or probably effective and should be considered for migraine prevention.

The Institute for Clinical Systems Improvement (ICSI) Diagnosis and Treatment of Headache guideline provides a recommendation for the prophylactic therapy trial duration. There is usually a latency of at least 3 to 6 weeks between the initiation of medication and recognizable efficacy. Often, an 8- to 12-week trial is necessary, allowing an adequate period for drug titration to a dosage likely to attain efficacy. Most prophylactic medications should be started in a low dose and titrated to a therapeutic dose to minimize side effects and maintained at target dose for 8-12 weeks to obtain maximum efficacy. It is also common for initial side effects to subside after continued therapy. Therefore, for coverage of the requested drug, patients with migraine headache must have had a trial for eight weeks, or had an intolerance or contraindication that would prohibit eight-week trials.

The recommended dosage of Aimovig is 70mg injected subcutaneously once monthly. Some patients may benefit from a dosage of 140mg injected subcutaneously once monthly. Aimovig is intended for patient self-administration. Aimovig is supplied as SureClick Autoinjector or Prefilled Syringe in a pack of one 70mg/mL or one 140mg/mL single-dose prefilled autoinjector or syringe, and was previously available in a pack of two 70mg/mL single-dose prefilled autoinjectors or syringes. Therefore, the limit is set at a quantity of one 140mg/mL autoinjector or syringe and two 70mg/mL autoinjectors or syringes per month.

Two subcutaneous dosing options of Ajovy are available to administer the recommended dosage: 225mg monthly, or 675mg every 3 months (quarterly) administered as three consecutive subcutaneous injections of 225mg each.
When switching dosage options, administer the first dose of the new regimen on the next scheduled date of administration. Ajovy may be administered by healthcare professionals, patients, and/or caregivers. Ajovy is supplied as a carton of one 225mg/1.5mL single-dose prefilled syringe. Therefore, the limit is set at a quantity of 3 prefilled syringes per a 3 month period.

The recommended dosage of Emgality for migraines is 240mg (two consecutive subcutaneous injections of 120mg each) once as a loading dose, followed by monthly doses of 120mg injected subcutaneously. Emgality is intended for patient self-administration. Emgality is supplied in a carton of one 120mg/mL single-dose prefilled pen or single-dose prefilled syringe and in a carton of two.

The efficacy of Aimovig was evaluated as a preventive treatment of episodic or chronic migraine in three randomized, double-blind, placebo-controlled studies: two studies in patients with episodic migraine (4 to 14 migraine days per month) and one study in patients with chronic migraine (≥15 headache days per month with ≥ 8 migraine days per month). The efficacy of Ajovy was evaluated as a preventive treatment of episodic or chronic migraine in three multicenter, randomized, 3-month, double-blind, placebo-controlled studies: one study in patients with episodic migraine (<15 headache days per month) and one study in patients with chronic migraine (≥15 headache days per month). The efficacy of Emgality was evaluated as a preventive treatment of episodic or chronic migraine in three multicenter, randomized, double-blind, placebo-controlled studies: two 6-month studies in patients with episodic migraine and one 3-month study in patients with chronic migraine. The primary efficacy endpoints were the mean change from baseline in the monthly average number of migraine days during the 3-6 month treatment period. Therefore, after 3 months of therapy the patient should have improvement in the change from baseline in migraine days for approval. The duration of approval for initial starts will be 3 months and for continuation will be 12 months. The duration of approval for initial starts for the REG 3160-C criteria is 12 months to comply with regulatory standards.

Cluster headaches are an extremely debilitating primary headache disorder. Episodic cluster headache is six times more common than the chronic form. Patients with the episodic cluster headaches have at least two cluster periods of at least one week but less than one year, with remission for at least one month. The American Headache Society (AHS) 2016 guideline update for the treatment of cluster headaches states and the 2010 American Academy of Neurology (AAN) recommendations for the treatment of cluster headache state that the following medications are established as effective for acute treatment of cluster headaches: sumatriptan subcutaneous, zolmitriptan nasal spray, and oxygen. Additionally, the following medications are probably effective: sumatriptan nasal spray and zolmitriptan oral. The American Academy of Family Physicians (AAFP) also recommends triptans (subcutaneous or nasal sumatriptan and nasal or oral zolmitriptan) and supplemental oxygen for first line abortive therapies for cluster headaches. Other therapies for acute treatment (e.g. octreotide, dihydroergotamine nasal spray, prednisone) are classified as possibly effective or insufficient evidence to make recommendation by the AHS and AAN for acute treatment of cluster headache. The AAFP also states there is weaker supporting evidence for intranasal lidocaine, octreotide, dihydroergotamine, and prednisone for acute treatment of cluster headache. Therefore, the trial drug criteria options will include the drugs the AAN and AHS guideline recommended as effective and should be offered or probably effective and should be considered for treatment of episodic cluster headache.

The recommended dosage of Emgality for cluster headaches is 300 mg (three consecutive subcutaneous injections of 100 mg each) at the onset of the cluster period, and then monthly until the end of the cluster period. Emgality is intended for patient self-administration.

If a dose of Emgality is missed during a cluster period, administer as soon as possible. Thereafter, Emgality can be scheduled monthly form the date of the last dose until the end of the cluster period.

Emgality is supplied in a carton of three 100mg/mL single-dose prefilled syringes.

The efficacy of Emgality was evaluated for the treatment of episodic cluster headache in a randomized, 8-week double-blind, placebo-controlled study. The primary efficacy endpoint was the mean change from baseline in weekly cluster headache attack frequency across Weeks 1 to 3. A secondary endpoint was the percentage of patients who achieved a response (defined as a reduction from baseline of 50% or greater in the weekly cluster headache attack frequency) at Week 3. Therefore, after 3 weeks of therapy the patient should have improvement in the change from baseline in weekly cluster headache attack frequency. Thus, when Emgality is prescribed for the treatment of cluster headache in adults, the duration of approval for initial starts will be 1 month and for continuation will be 12 months.
REFERENCES


CRITERIA FOR APPROVAL

1. Is the requested drug being prescribed for the preventive treatment of migraine in an adult patient? [If no, then skip to question 10.]
   - Yes
   - No

2. Has the patient received at least 3 months of treatment with the requested drug? [If no, then skip to question 5.]
   - Yes
   - No

3. Has the patient had a reduction in migraine days per month from baseline? [If no, then skip to question 10.]
   - Yes
   - No

CGRP Receptor Antagonists 2581-C, REG 3160-C 06-2019 ©2019 CVS Caremark. All rights reserved.
4. Does the patient require more than the plan allowance of any of the following: A) 1 injection of 140mg or 2 injections of 70mg per month of Aimovig, B) 3 injections (225mg each) per 3 months of Ajovy, C) 1 injection (120mg) per month of Emgality? [No further questions.]

[RPh Note: If yes, then deny and enter a partial approval per Limit Quantity Chart.]

Yes

No

5. Has the patient experienced an inadequate treatment response with an 8-week trial of any of the following: Antiepileptic drugs (AEDs) (e.g., divalproex sodium, topiramate, valproate sodium), Beta-adrenergic blocking agents (e.g., metoprolol, propranolol, timolol, atenolol, nadolol), Antidepressants (e.g., amitriptyline, venlafaxine)?

Yes

No

If yes, then skip to question 7.

6. Has the patient experienced an intolerance or have a contraindication that would prohibit an 8-week trial of any of the following: Antiepileptic drugs (AEDs) (e.g., divalproex sodium, topiramate, valproate sodium), Beta-adrenergic blocking agents (e.g., metoprolol, propranolol, timolol, atenolol, nadolol), Antidepressants (e.g., amitriptyline, venlafaxine)?

Yes

No

If yes, then skip to question 7.

7. Is this request for Aimovig or Ajovy?

Yes

No

If no, then skip to question 9.

8. Does the patient require more than the plan allowance of any of the following: A) 1 injection of 140mg or 2 injections of 70mg per month of Aimovig, B) 3 injections (225mg each) per 3 months of Ajovy? [No further questions.]

[RPh Note: If yes, then deny and enter a partial approval per Limit Quantity Chart.]

Yes

No

9. Does the patient require more than the plan allowance of 4 injections (120mg each) per first 3 months of Emgality (i.e., loading dose of 2 injections followed by 1 injection per month)?

Yes

No

[RPh Note: If yes, then deny and enter a partial approval per mapping guidelines.]

10. Is the request for Emgality 100mg for the treatment of episodic cluster headache in an adult patient?

Yes

No

11. Has the patient received at least 3 weeks of treatment with the requested drug?

Yes

No

If no, then skip to question 14.

12. Has the patient had a reduction in weekly cluster headache attack frequency from baseline?

Yes

No

13. Does the patient require more than the plan allowance of 3 injections (100mg each) per month of Emgality?

Yes

No

[No further questions.]

[RPh Note: If yes, then deny and enter a partial approval per Limit Quantity Chart.]

14. Has the patient experienced an inadequate treatment response with sumatriptan (subcutaneous or nasal) or zolmitriptan (nasal or oral)?

Yes

No

[If yes, then skip to question 16.]

15. Has the patient experienced intolerance or contraindication to sumatriptan (subcutaneous or nasal) or zolmitriptan (nasal or oral)?

Yes

No
16. Does the patient require more than the plan allowance of 3 injections (100mg each) per month of Emgality?  

Yes  No

[RPh Note: If yes, then then deny and enter a partial approval per Limit Quantity Chart.]

---

### Mapping Instructions (2581-C)

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Go to 2</td>
<td>Go to 10</td>
</tr>
<tr>
<td>2. Go to 3</td>
<td>Go to 5</td>
</tr>
<tr>
<td>3. Go to 4</td>
<td>Deny</td>
</tr>
<tr>
<td>4. Deny</td>
<td>Approve, 12 months, See Limit Quantity Chart</td>
</tr>
</tbody>
</table>

#### DENIAL REASONS – DO NOT USE FOR MEDICARE PART D

- You do not meet the requirements of your plan. Your plan covers this drug when you have fewer migraine days per month since starting the drug. Your request has been denied based on the information we have. [Short Description: Continuation of therapy, Inadequate response to treatment]
- You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 2 autoinjectors or syringes/month of Aimovig 70mg, or 1 autoinjector or syringe/month of Aimovig 140mg - 3 syringes/3 months of Ajovy 225mg - 1 syringe or pen/month of Emgality 120mg You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]

---

5. Go to 7  Go to 6

6. Go to 7  Deny

Your plan covers this drug when you have tried any of the following for 8 weeks and it did not work for you, or you cannot take them: Antiepileptic drugs (AED) (e.g., divalproex sodium, topiramate, valproate sodium), Beta-adrenergic blocking agents (e.g., metoprolol, propranolol, timolol, atenolol, nadolol), Antidepressants (e.g., amitriptyline, venlafaxine).

Your request has been denied based on the information we have. [Short Description: No inadequate response with an 8 week trial, intolerance or contraindication to any of the following: Antiepileptic drugs (AEDs) (e.g., divalproex sodium, topiramate, valproate sodium), Beta-adrenergic blocking agents (e.g., metoprolol, propranolol, timolol, atenolol, nadolol); Antidepressants (e.g., amitriptyline, venlafaxine)]

7. Go to 8  Got to 9

8. Deny | Approve, 3 months, See Limit Quantity Chart

You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 2 autoinjectors or syringes/month of Aimovig 70mg, or 1 autoinjector or syringe/month of Aimovig 140mg - 3 syringes/3 months of Ajovy 225mg
<table>
<thead>
<tr>
<th>MAP 169 - C</th>
<th>CGRP Receptor Antagonists 2581-C, REG 3160-C 06-2019 ©2019 CVS Caremark. All rights reserved. This document contains confidential and proprietary information of CVS Caremark and cannot be reproduced, distributed or printed without written permission from CVS Caremark. This document contains references to brand-name prescription drugs that are trademarks or registered trademarks of pharmaceutical manufacturers not affiliated with CVS Caremark.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Other drugs from the verbiage.</strong></td>
<td>You have been approved for the maximum quantity that your plan covers for a duration of 3 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]</td>
</tr>
<tr>
<td>9. Deny</td>
<td>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 4 syringes or pens per first 3 months of Emgality 120mg (i.e., 2 injections for the first dose then 1 injection/month). You have been approved for the maximum quantity that your plan covers for a duration of 3 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]</td>
</tr>
<tr>
<td>10. Go to 11</td>
<td>Deny You do not meet the requirements of your plan. Your plan covers this drug when you are an adult and meet any of the following conditions: - You are using it for preventive treatment of migraine - You are requesting Emgality 100mg for the treatment of cluster headaches Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]</td>
</tr>
<tr>
<td>11. Go to 12</td>
<td>Go to 14</td>
</tr>
<tr>
<td>12. Go to 13</td>
<td>Deny You do not meet the requirements of your plan. Your plan covers this drug when you have fewer weekly cluster headache attacks since starting the drug. Your request has been denied based on the information we have. [Short Description: Continuation of therapy, Inadequate response to treatment]</td>
</tr>
<tr>
<td>13. Deny</td>
<td>Approve, 12 months, See Limit Quantity Chart You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 3 syringes/month of Emgality 100mg You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]</td>
</tr>
<tr>
<td>14. Go to 16</td>
<td>Go to 15</td>
</tr>
<tr>
<td>15. Go to 16</td>
<td>Deny You do not meet the requirements of your plan. Your plan covers this drug when you have tried any of the following and it did not work for you, or you cannot take them: sumatriptan (injection or nasal spray) or zolmitriptan (nasal spray or tablet). Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance or contraindication to any of the following: sumatriptan (injection or nasal spray) or zolmitriptan (nasal spray or tablet).]</td>
</tr>
<tr>
<td>16. Deny</td>
<td>Approve, 1 month, See Limit Quantity Chart You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 3 syringes/month of Emgality 100mg You have been approved for the maximum quantity that your plan covers for a duration of 1 month. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]</td>
</tr>
</tbody>
</table>

### Mapping Instructions (3160-C)

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
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<tbody>
<tr>
<td><strong>DENIAL REASONS – DO NOT USE FOR MEDICARE PART D</strong></td>
<td></td>
</tr>
<tr>
<td>1. Go to 2</td>
<td>Go to 10</td>
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</tr>
<tr>
<td>12. Go to 13</td>
<td>Deny</td>
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<tr>
<td>13. Deny</td>
<td>Approve, 12 months, See Limit Quantity Chart</td>
</tr>
<tr>
<td>14. Go to 16</td>
<td>Go to 15</td>
</tr>
<tr>
<td>15. Go to 16</td>
<td>Deny</td>
</tr>
<tr>
<td>16. Deny</td>
<td>Approve, 1 month, See Limit Quantity Chart</td>
</tr>
</tbody>
</table>

### LIMIT QUANTITY

**Migraine:**

<table>
<thead>
<tr>
<th>Drug</th>
<th>1 Month Limit*</th>
<th>3 Month Limit*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aimovig 70mg (erenumab-aooe injection)</td>
<td>2mL (2 autoinjectors or syringes x 1mL each) / 25 days</td>
<td>6mL (6 autoinjectors or syringes x 1mL each) / 75 days</td>
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<tr>
<td>Aimovig 140mg (erenumab-aooe injection)</td>
<td>1mL (1 autoinjector or syringe x 1mL each) / 25 days</td>
<td>3mL (3 autoinjectors or syringes x 1mL each) / 75 days</td>
</tr>
<tr>
<td>Emgality 120mg (galcanezumab-gnlm injection)</td>
<td>1mL (1 syringe or pen x 1mL each) / 25 days</td>
<td>3mL (3 syringes or pens x 1mL each) / 75 days</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug</th>
<th>1 Month Limit and 3 Month Limit*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ajovy</td>
<td>4.5mL (3 syringes x 1.5 mL each) / 75 days</td>
</tr>
</tbody>
</table>

**Cluster Headache:**
<table>
<thead>
<tr>
<th>Emgality</th>
<th>1 Month Limit*</th>
<th>3 Month Limit*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emgality 100mg (galcanezumab-gnlm injection)</td>
<td>3mL (3 syringe x 1mL each)/ 25 days</td>
<td>9mL (9 syringe x 1mL each)/ 75 days</td>
</tr>
</tbody>
</table>

*The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.
SPECIALTY GUIDELINE MANAGEMENT

CHOLBAM (cholic acid)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Cholbam is indicated for:
1. Treatment of bile acid synthesis disorders due to single enzyme defects (SEDs)
2. Adjunctive treatment of peroxisomal disorders (PDs) including Zellweger spectrum disorders in patients who exhibit manifestations of liver disease, steatorrhea or complications from decreased fat soluble vitamin absorption

Limitation of use: The safety and effectiveness of Cholbam on extrahepatic manifestations of bile acid synthesis disorders due to SEDs or PDs including Zellweger spectrum disorders have not been established.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Bile acid synthesis disorders due to single enzyme defects (SEDs)
Authorization of 6 months may be granted for treatment of bile acid synthesis disorders due to single enzyme defects when the diagnosis is confirmed by mass spectrometry or other biochemical testing or genetic testing.

B. Peroxisomal disorders (PDs) including Zellweger spectrum disorders
Authorization of 6 months may be granted for adjunctive treatment of peroxisomal disorders when the diagnosis is confirmed by mass spectrometry or other biochemical testing or genetic testing.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet additional authorization criteria below:

A. Bile acid synthesis disorders due to SEDs
Authorization of 12 months may be granted to members who have achieved and maintained improvement in liver function.

B. Peroxisomal disorders (PDs) including Zellweger spectrum disorders
Authorization of 12 months may be granted to members continuing adjunctive treatment with Cholbam who have achieved and maintained improvement in liver function.
IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

CIMZIA (certolizumab pegol)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Moderately to severely active rheumatoid arthritis (RA)
   2. Active psoriatic arthritis (PsA)
   3. Active ankylosing spondylitis (AS)
   4. Moderately to severely active Crohn’s disease (CD)
   5. Moderate to severe plaque psoriasis (PsO)

B. Compendial Use
   Axial spondyloarthritis

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active rheumatoid arthritis (RA)
   1. Authorization of 24 months may be granted for members who have previously received Cimzia or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) indicated for moderately to severely active rheumatoid arthritis.
   2. Authorization of 24 months may be granted for treatment of moderately to severely active RA when any of the following criteria is met:
      a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
      b. Member has an intolerance or contraindication to methotrexate (see Appendix A).

B. Active psoriatic arthritis (PsA)
   Authorization of 24 months may be granted for treatment of active psoriatic arthritis (PsA).

C. Active ankylosing spondylitis (AS) and axial spondyloarthritis
   1. Authorization of 24 months may be granted for members who have previously received Cimzia or any other biologic DMARD indicated for active ankylosing spondylitis.
   2. Authorization of 24 months may be granted for treatment of active ankylosing spondylitis and axial spondyloarthritis when any of the following criteria is met:
      a. Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs).
      b. Member has an intolerance or contraindication to two or more NSAIDs.
D. Moderately to severely active Crohn’s disease (CD)
   1. Authorization of 24 months may be granted for members who have previously received Cimzia or any other biologic indicated for the treatment of Crohn’s disease.

   2. Authorization of 24 months may be granted for treatment of moderately to severely active CD when the member has an inadequate response, intolerance or contraindication to at least one conventional therapy option (see Appendix B).

E. Moderate to severe plaque psoriasis (PsO)
   1. Authorization of 24 months may be granted for members who have previously received Cimzia, Otezla, or any other biologic DMARD indicated for the treatment of moderate to severe plaque psoriasis.

   2. Authorization of 24 months may be granted for treatment of moderate to severe plaque psoriasis when all of the following criteria are met:
      a. At least 5% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
      b. Member meets any of the following criteria:
         i. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or a pharmacologic treatment with methotrexate, cyclosporine or acitretin.
         ii. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine or acitretin (see Appendix C).
         iii. Member has severe psoriasis that warrants a biologic DMARD as first-line therapy.

III. CONTINUATION OF THERAPY

   Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Cimzia as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

   For all indications: Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB).

   Note: Members who have received Cimzia or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) are exempt from requirements related to TB screening in this Policy.

V. APPENDICES

   Appendix A: Examples of Contraindications to Methotrexate
   1. Alcoholism, alcoholic liver disease or other chronic liver disease
   2. Breastfeeding
   3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
   4. Elevated liver transaminases
   5. History of intolerance or adverse event
   6. Hypersensitivity
   7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
   8. Myelodysplasia
9. Pregnancy or planning pregnancy  
10. Renal impairment  
11. Significant drug interaction

**Appendix B: Examples of Conventional Therapy Options for CD**

1. Mild to moderate disease – induction of remission:  
   a. Oral budesonide  
   b. Alternatives: metronidazole, ciprofloxacin, rifaximin

2. Mild to moderate disease – maintenance of remission:  
   a. Azathioprine, mercaptopurine  
   b. Alternatives: oral budesonide, methotrexate intramuscularly (IM) or subcutaneously (SC), sulfasalazine

3. Moderate to severe disease – induction of remission:  
   a. Prednisone, methylprednisolone intravenously (IV)  
   b. Alternatives: methotrexate IM or SC

4. Moderate to severe disease – maintenance of remission:  
   a. Azathioprine, mercaptopurine  
   b. Alternative: methotrexate IM or SC

5. Perianal and fistulizing disease – induction of remission:  
   a. Metronidazole ± ciprofloxacin, tacrolimus

6. Perianal and fistulizing disease – maintenance of remission:  
   a. Azathioprine, mercaptopurine  
   b. Alternative: methotrexate IM or SC

**Appendix C: Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin.**

1. Alcoholism, alcoholic liver disease or other chronic liver disease  
2. Breastfeeding  
3. Drug interaction  
4. Cannot be used due to risk of treatment-related toxicity  
5. Pregnancy or planning pregnancy  
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

**VI. REFERENCES**


SPECIALTY GUIDELINE MANAGEMENT

CINQAIR (reslizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Cinqair is indicated for the add-on maintenance treatment of patients with severe asthma aged 18 years and older with an eosinophilic phenotype.

Limitations of Use:
- Not for treatment of other eosinophilic conditions
- Not for the relief of acute bronchospasm or status asthmaticus

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Member’s chart or medical record showing baseline blood eosinophil count (initial request only)

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 6 months may be granted for treatment of asthma when all of the following criteria are met:

A. Member is 18 years of age or older.
B. Member has baseline blood eosinophil count of at least 400 cells per microliter.
C. Member has inadequate asthma control (e.g., hospitalization or emergency medical care visit within the past year) despite current treatment with both of the following medications at optimized doses:
   1. Inhaled corticosteroid
   2. Additional controller (long acting beta2-agonist, leukotriene modifier, or sustained-release theophylline)
D. Member will not use Cinqair as monotherapy.
E. Member does not currently smoke.
F. Member will not use Cinqair concomitantly with other biologics (e.g., Dupixent, Fasenra, Nucala, Xolair).

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for treatment of asthma when all of the following criteria are met:

A. Member is 18 years of age or older.
B. Asthma control has improved on Cinqair treatment as demonstrated by a reduction in the frequency and/or severity of symptoms and exacerbations.
C. Member will not use Cinqair as monotherapy.
D. Member does not currently smoke.
E. Member will not use Cinqair concomitantly with other biologics (e.g., Dupixent, Fasenra, Nucala, Xolair).

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

CINRYZE (C1 esterase inhibitor [human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   Routine prophylaxis against angioedema attacks in adults, adolescents and pediatric patients (6 years of age or older) with hereditary angioedema (HAE)

B. Compendial Uses
   Treatment of acute HAE attacks

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Indefinite authorization may be granted for treatment and prevention of hereditary angioedema attacks when either of the following criteria is met:

A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing.

B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
   1. Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing, or
   2. Member has a family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES


ENHANCED SPECIALTY GUIDELINE MANAGEMENT

CINRYZE (C1 esterase inhibitor [human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Routine prophylaxis against angioedema attacks in adults, adolescents and pediatric patients (6 years of age or older) with hereditary angioedema (HAE)

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review: C4 levels and C1 inhibitor functional and antigenic protein levels.

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for prevention of hereditary angioedema attacks when either of the following criteria is met:

A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing.
B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
   1. Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing, or
   2. Member has a family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy when all of the following criteria are met:

A. Member meets the criteria for initial approval.
B. Member has experienced reduction in frequency, severity and duration of attacks since starting treatment.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

COAGADEX (coagulation Factor X [human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Coagadex is indicated in adults and children with hereditary Factor X deficiency for:
A. Routine prophylaxis to reduce the frequency of bleeding episodes
B. On-demand treatment and control of bleeding episodes
C. Perioperative management of bleeding in patients with mild and moderate hereditary Factor X deficiency.

Limitation of Use:
Perioperative management of bleeding in major surgery in patients with severe hereditary Factor X deficiency has not been studied.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Hereditary Factor X Deficiency
A. Indefinite authorization may be granted for prophylaxis to reduce the frequency of bleeding episodes
B. Indefinite authorization may be granted for on-demand treatment and control of bleeding episodes.
C. Authorization of 1 month may be granted for perioperative management of bleeding in members with mild or moderate hereditary Factor X deficiency (i.e., baseline Factor X assay level ≥ 1%).

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

COMETRIQ (cabozantinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
   Treatment of progressive, metastatic medullary thyroid cancer (MTC).

B. Compendial Uses
   1. Follicular, Hurthle cell, and papillary thyroid carcinoma
   2. Non-small cell lung cancer with RET gene arrangements

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of RET gene rearrangement documentation is necessary to initiate the prior authorization review for the indication of non-small cell lung cancer.

III. CRITERIA FOR INITIAL APPROVAL

A. Thyroid carcinoma (follicular, Hürthle cell, papillary)
   Authorization of 12 months may be granted for the treatment of radioiodine refractory follicular, Hürthle cell, or papillary thyroid carcinoma.

B. Medullary thyroid carcinoma
   Authorization of 12 months may be granted for the treatment of medullary thyroid carcinoma.

C. Non-small cell lung cancer (NSCLC)
   Authorization of 12 months may be granted for the treatment of NSCLC with RET gene rearrangements.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in Section III when there is no evidence of unacceptable toxicity or disease progression on the current regimen.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

COPAXONE (glatiramer acetate)
GLATOPA (glatiramer acetate)
glatiramer acetate

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Copaxone is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.
2. Glatopa and glatiramer acetate are indicated for the treatment of patients with relapsing forms of multiple sclerosis.

B. Compendial Use
Relapsing-remitting multiple sclerosis, including patients who have experienced a first clinical episode and have MRI features consistent with multiple sclerosis

All other indications are considered experimental/investigational and are not covered benefits.

II. CRITERIA FOR INITIAL APPROVAL

A. Relapsing forms of multiple sclerosis
Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse)

B. Clinically isolated syndrome
Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome of multiple sclerosis.

III. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted for members who are experiencing disease stability or improvement while receiving Copaxone, Glatopa, or glatiramer acetate.

IV. OTHER CRITERIA

Members will not use Copaxone, Glatopa, or glatiramer acetate concomitantly with other medications used for the treatment of multiple sclerosis, excluding Ampyra.
V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

COPIKTRA (duvelisib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL)
   Copiktra is indicated for the treatment of adult patients with relapsed or refractory CLL or SLL after at least two prior therapies.

B. Follicular lymphoma
   Copiktra is indicated for the treatment of adult patients with relapsed or refractory FL after at least two prior systemic therapies.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL)
   Authorization of 12 months may be granted for treatment of relapsed or refractory CLL/SLL when the member has received at least two prior therapies.

B. Follicular lymphoma (FL)
   Authorization of 12 months may be granted for treatment of relapsed or refractory FL when the member has received at least two prior therapies.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

COSENTYX (secukinumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
1. Moderate to severe plaque psoriasis (PsO)
2. Active psoriatic arthritis (PsA)
3. Active ankylosing spondylitis (AS)

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderate to severe plaque psoriasis (PsO)
   1. Authorization of 24 months may be granted for members who are 18 years of age or older who have previously received Cosentyx, Otezla, or any other biologic DMARD indicated for the treatment of moderate to severe plaque psoriasis.

   2. Authorization of 24 months may be granted for treatment of moderate to severe plaque psoriasis in members who are 18 years of age or older when all of the following criteria are met:
      a. At least 5% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
      b. Member meets any of the following criteria:
         i. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
         ii. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine or acitretin (see Appendix A).
         iii. Member has severe psoriasis that warrants a biologic DMARD as first-line therapy.

B. Active psoriatic arthritis (PsA)
   Authorization of 24 months may be granted for treatment of active psoriatic arthritis in members who are 18 years of age or older.

C. Active ankylosing spondylitis (AS)
   1. Authorization of 24 months may be granted for members who are 18 years of age or older who have previously received Cosentyx or any other biologic DMARD indicated for active ankylosing spondylitis.

   2. Authorization of 24 months may be granted for treatment of active ankylosing spondylitis in members 18 years of age or older when any of the following criteria is met:
a. Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs).
b. Member has an intolerance or contraindication to two or more NSAIDs.

III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 4 months of therapy with Cosentyx as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB).

Note: Members who have received Cosentyx or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) are exempt from requirements related to TB screening in this Policy.

V. APPENDIX

Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin.
1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Drug interaction
4. Cannot be used due to risk of treatment-related toxicity
5. Pregnancy or planning pregnancy (male or female)
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VI. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

COTELLIC (cobimetinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Cotellic is indicated for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, in combination with vemurafenib.

B. Compendial Uses
1. Glioma, BRAF V600 activating mutation-positive
2. Meningioma, BRAF V600 activating mutation-positive
3. Astrocytoma, BRAF V600 activating mutation-positive
4. Brain metastases with melanoma

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of BRAF mutation documentation is necessary to initiate the prior authorization review for applicable indications as outlined in section III.

III. CRITERIA FOR INITIAL APPROVAL

A. Melanoma
Authorization for 12 months may be granted for treatment of unresectable or metastatic melanoma (including brain metastases with melanoma) when all of the following criteria are met:
1. Cotellic is used in combination with vemurafenib (Zelboraf)
2. Tumor is positive for BRAF V600E or V600K mutation

B. Central Nervous System Cancer
Authorization of 12 months may be granted for treatment of BRAF V600 mutation-positive gliomas, meningiomas, or astrocytomas.

IV. CONTINUATION OF THERAPY
Authorization of 12 months may be granted for continuation of therapy for an indication outlined in Section III when there is no evidence of unacceptable toxicity or disease progression on the current regimen.

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

CRYSVITA (burosumab-twza)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Crysvita is indicated for the treatment of X-linked hypophosphatemia (XLH) in adult and pediatric patients 1 year of age and older.

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

At least one of the following information is necessary to initiate the prior authorization review:

A. Genetic testing results confirming the member has a PHEX (phosphate regulating gene with homology to endopeptidases located on the X chromosome) mutation

B. Genetic testing results confirming a PHEX mutation in a directly related family member with appropriate X-linked inheritance

C. Lab test results confirming the member’s serum fibroblast growth factor 23 (FGF23) level is greater than 30 pg/ml

III. CRITERIA FOR INITIAL APPROVAL

X-linked hypophosphatemia

Authorization of 12 months may be granted for treatment of X-linked hypophosphatemia when one of the following criteria is met:

A. Genetic testing was conducted to confirm a PHEX mutation in the member and genetic testing results were submitted confirming diagnosis.

B. Genetic testing was conducted to confirm a PHEX mutation in a directly related family member with appropriate X-linked inheritance and genetic testing results were submitted confirming diagnosis.

C. Member’s FGF23 level is greater than 30 pg/ml and lab test results were submitted confirming diagnosis.

IV. CONTINUATION OF THERAPY

Authorization of 12 months will be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who are currently receiving the requested medication through a paid pharmacy or medical benefit and who are experiencing benefit from therapy as evidenced by disease improvement or disease stability.
V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

CYRAMZA (ramucirumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Gastric Cancer: Cyramza as a single agent, or in combination with paclitaxel, is indicated for the treatment of patients with advanced or metastatic, gastric or gastro-esophageal junction (GEJ) adenocarcinoma with disease progression on or after prior fluoropyrimidine-or platinum-containing chemotherapy.
   2. Non-Small Cell Lung Cancer (NSCLC): Cyramza, in combination with docetaxel, is indicated for the treatment of patients with metastatic NSCLC with disease progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Cyramza.
   3. Colorectal Cancer: Cyramza, in combination with FOLFIRI (irinotecan, folinic acid, and 5-fluorouracil), is indicated for the treatment of patients with metastatic colorectal cancer with disease progression on or after prior therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine.

B. Compendial Uses
   1. Esophageal adenocarcinoma
   2. Colorectal cancer, advanced
   3. Hepatobiliary cancer

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Gastric, Gastro-esophageal Junction (GEJ), and Esophageal Adenocarcinoma
   Authorization of 12 months may be granted for treatment of gastric, gastro-esophageal junction (GEJ), and esophageal adenocarcinoma.

B. Non-Small Cell Lung Cancer (NSCLC)
   Authorization of 12 months may be granted for treatment of metastatic NSCLC.

C. Colorectal Cancer
   Authorization of 12 months may be granted for treatment of advanced or metastatic colorectal cancer.

D. Hepatobiliary cancer
   Authorization of 12 months may be granted for treatment of hepatobiliary cancer.
III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

CYSTAGON (cysteamine bitartrate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Cystagon is indicated for the management of nephropathic cystinosis in children and adults.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Nephropathic cystinosis
Indefinite authorization may be granted for treatment of nephropathic cystinosis when the diagnosis of cystinosis was confirmed by the presence of increased cystine concentration in leukocytes or by genetic testing.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

CYSTARAN (cysteamine ophthalmic solution)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Cystaran is indicated for the treatment of corneal cystine crystal accumulation in patients with cystinosis.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Cystinosis

Indefinite authorization may be granted for treatment of corneal cystine crystal accumulation when all of the following criteria are met:

A. Diagnosis of cystinosis was confirmed by the presence of increased cystine concentration in leukocytes or by genetic testing

B. Member has corneal cystine crystal accumulation

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

DAKLINZA (daclatasvir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Daklinza is indicated for use with sofosbuvir, with or without ribavirin, for the treatment of patients with chronic hepatitis C virus (HCV) genotype 1 or genotype 3 infection.

Limitations of Use:

Sustained virologic response (SVR12) rates are reduced in HCV genotype 3-infected patients with cirrhosis receiving Daklinza in combination with sofosbuvir for 12 weeks.

B. Compendial Uses

Chronic hepatitis C genotype 2, 4, 5 or 6 infection

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR APPROVAL

A. Chronic hepatitis C virus infection, in combination with Sovaldi

1. Genotype 1 infection

a. Authorization of up to 12 weeks total may be granted for treatment-naive members without cirrhosis or with compensated cirrhosis.

b. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with peginterferon alfa (PEG-IFN) and ribavirin (RBV).

2. Genotype 2 infection

a. Authorization of up to 12 weeks total may be granted for treatment-naive members without cirrhosis.

b. Authorization of up to 24 weeks total may be granted for treatment-naive members with compensated cirrhosis.

c. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with PEG-IFN and RBV.

d. Authorization of up to 24 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV.

3. Genotype 3 infection

a. Authorization of up to 12 weeks total may be granted for treatment-naive members without cirrhosis.

b. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with PEG-IFN and RBV.

C. Authorization of up to 24 weeks total may be granted for treatment-naive members with compensated cirrhosis.
4. ** Decompensated cirrhosis (Child Turcotte Pugh [CTP] class B or C)**
   Authorization of up to 24 weeks total may be granted for members with HCV genotype 1, 2, 3 or 4 infection and documented anemia (baseline hemoglobin [Hgb] below 10 g/dL) or RBV ineligibility (see Section III).

B. **Chronic hepatitis C virus, in combination with Sovaldi and Ribavirin**
   1. **Genotype 3 infection**
      a. Authorization of up to 24 weeks total may be granted for treatment-naive members with compensated cirrhosis.
      b. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with PEG-IFN and RBV and have the Y93H substitution associated with daclatasvir resistance.

2. ** Decompensated cirrhosis (CTP class B or C)**
   Authorization of up to 12 weeks total may be granted for members with HCV genotype 1, 2, 3 or 4 infection.

3. ** Recurrent HCV infection post liver transplantation**
   a. Authorization of up to 12 weeks total may be granted for members with recurrent HCV genotype 1, 2, or 3 infection post liver transplantation.
   b. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have recurrent HCV genotype 4, 5 or 6 infection post liver transplantation.

4. ** Kidney transplant recipients**
   Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have HCV genotype 2, 3, 5, or 6 infection.

C. **HCV and HIV coinfection**
   Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A or B above are met.

III. **CONTINUATION OF THERAPY**

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. **APPENDIX: RIBAVIRIN INELIGIBILITY**

RBV ineligibility is defined as one or more of the below:
- Intolerance to RBV
- Pregnant female or male whose female partner is pregnant
- Hemoglobinopathy
- Coadministration with didanosine
- History of significant or unstable cardiac disease

V. **REFERENCES**
Specialty Guideline Management

DARZALEX (daratumumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Darzalex is indicated:
A. in combination with bortezomib, melphalan and prednisone for the treatment of patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant.
B. in combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of patients with multiple myeloma who have received at least one prior therapy.
C. in combination with pomalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor.
D. as monotherapy, for the treatment of patients with multiple myeloma who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent.

All other indications are considered experimental/investigational and are not covered benefits.

II. CRITERIA FOR INITIAL APPROVAL

Multiple Myeloma
Authorization of 12 months may be granted for the treatment of multiple myeloma.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

DAURISMO (glasdegib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Daurismo is indicated, in combination with low-dose cytarabine, for the treatment of newly-diagnosed acute myeloid leukemia (AML) in adult patients who are 75 years of age or older or who have comorbidities that preclude use of intensive induction chemotherapy.

Limitation of Use: Daurismo has not been studied in patients with the comorbidities of severe renal impairment or moderate-to-severe hepatic impairment.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Newly-diagnosed AML

Authorization of 12 months may be granted for treatment of newly-diagnosed AML when any of the following criteria is met:
A. Member is 75 years of age or older.
B. Member has comorbidities that preclude treatment with intensive induction chemotherapy.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

DACOGEN (decitabine)
decitabine (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Myelodysplastic syndromes (MDS): Dacogen is indicated for treatment of patients with myelodysplastic syndromes (MDS) including previously treated and untreated, de novo and secondary MDS of all French-American-British subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, refractory anemia with excess blasts in transformation, and chronic myelomonocytic leukemia) and intermediate-1, intermediate-2, and high-risk International Prognostic Scoring System groups.

B. Compendial Uses

1. Chronic myeloid leukemia (CML)
2. Acute myeloid leukemia (AML)
3. Accelerated phase or blast phase myelofibrosis
4. Lower risk myelodysplastic syndromes (MDS) associated with thrombocytopenia, neutropenia, symptomatic anemia, or increased marrow blasts

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Myelodysplastic Syndromes (MDS)
Authorization of 12 months may be granted for the treatment of MDS.

B. Chronic myeloid leukemia (CML)
Authorization of 12 months may be granted for the treatment of CML.

C. Acute Myeloid Leukemia (AML)
Authorization of 12 months may be granted for the treatment of AML.

D. Accelerated Phase or Blast Phase Myelofibrosis
Authorization of 12 months may be granted for the treatment of accelerated phase or blast phase myelofibrosis.

III. CONTINUATION OF THERAPY
All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

EXJADE (deferasirox; tablets for suspension)
JADENU (deferasirox; tablets, sprinkle granules)
deferasirox tablet for suspension

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Chronic iron overload due to blood transfusions (transfusional iron overload)
   2. Chronic iron overload in patients with non-transfusion-dependent thalassemia (NTDT) syndromes and with a liver iron concentration (LIC) of at least 5 milligrams of iron per gram of liver dry weight (mg Fe/g dw) and a serum ferritin greater than 300 mcg/L

B. Compendial Use
   Hereditary hemochromatosis

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Chronic Iron Overload due to Blood Transfusions (transfusional iron overload):
   1. Initial requests: pretreatment serum ferritin level
   2. Continuation requests: current serum ferritin level
B. Chronic Iron Overload in Patients with Non-transfusion Dependent Thalassemia Syndromes:
   1. Initial requests: pretreatment serum ferritin level and liver iron concentration
   2. Continuation requests: current serum ferritin level

III. CRITERIA FOR INITIAL APPROVAL

A. Chronic Iron Overload due to Blood Transfusions (transfusional iron overload)
   Authorization of 6 months may be granted for treatment of chronic iron overload due to blood transfusions when all of the following criteria are met:
   1. Pretreatment serum ferritin level is consistently greater than 1000 mcg/L.
   2. Dose of deferasirox/Exjade will not exceed 40 mg/kg, dose of Jadenu will not exceed 28 mg/kg.
   3. Member’s renal function has been evaluated.

B. Chronic Iron Overload in Patients with Non-transfusion Dependent Thalassemia Syndromes
Authorization of 6 months may be granted for treatment of chronic iron overload in members with non-transfusion dependent thalassemia syndromes when all of the following criteria are met:
1. Pretreatment serum ferritin level is greater than 300 mcg/L.
2. Pretreatment liver iron concentration (LIC) is at least 5 milligrams of iron per gram of liver dry weight (mg Fe/g dw).
3. Dose of deferasirox/Exjade will not exceed 20 mg/kg, dose of Jadenu will not exceed 14 mg/kg.
4. Member’s renal function has been evaluated.

C. Hereditary Hemochromatosis
Authorization of 6 months may be granted for treatment of hereditary hemochromatosis when both of the following criteria are met:
1. Phlebotomy is not an option (e.g., poor venous access, poor candidate due to underlying medical disorders) or the member had an unsatisfactory response to phlebotomy.
2. Member’s renal function has been evaluated.

IV. CONTINUATION OF THERAPY
Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when the following criteria are met:

A. Chronic Iron Overload due to Blood Transfusions (transfusional iron overload)
1. Member is experiencing benefit from therapy as evidenced by a decrease in serum ferritin levels as compared to pretreatment baseline.
2. Serum ferritin level is not consistently below 500 mcg/L.
3. Member’s renal function has been evaluated.

B. Chronic Iron Overload in Patients with Non-transfusion Dependent Thalassemia Syndromes
1. Member is experiencing benefit from therapy as evidenced by a decrease in serum ferritin levels as compared to pretreatment baseline.
2. Serum ferritin level is not consistently below 300 mcg/L.
3. Member’s renal function has been evaluated.

C. Hereditary Hemochromatosis
1. Member is experiencing benefit from therapy as evidenced by a decrease in serum ferritin levels as compared to pretreatment baseline.
2. Member’s renal function has been evaluated.

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

DESFERAL (deferoxamine)
deferoxamine mesylate (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
   Chronic iron overload due to transfusion-dependent anemias

B. Compendial Uses
   1. Aluminum toxicity in patients undergoing dialysis
   2. Hereditary hemochromatosis

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
Chronic iron overload due to transfusion-dependent anemias:
A. Initial requests: pretreatment serum ferritin level
B. Continuation requests: current serum ferritin level

III. CRITERIA FOR INITIAL APPROVAL

A. Chronic Iron Overload due to Transfusion-Dependent Anemias
   Authorization of 6 months may be granted for treatment of chronic iron overload due to transfusion-dependent anemias when the pretreatment serum ferritin level is consistently greater than 1000 mcg/L.

B. Aluminum toxicity in Patients Undergoing Dialysis
   Authorization of 6 months may be granted for treatment of aluminum toxicity in members undergoing dialysis.

C. Hereditary Hemochromatosis
   Authorization of 6 months may be granted for treatment of hereditary hemochromatosis when phlebotomy is not an option (e.g., poor candidate due to underlying medical disorders) or the member had an unsatisfactory response to phlebotomy.

IV. CONTINUATION OF THERAPY
Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when the following criteria are met:

A. **Chronic Iron Overload due to Transfusion-Dependent Anemias**
   Member is experiencing benefit from therapy as evidenced by a decrease in serum ferritin levels as compared to pretreatment baseline.

B. **Aluminum toxicity in Patients Undergoing Dialysis**
   Member is experiencing benefit from therapy as evidenced by any of the following:
   1. Decreased serum aluminum concentrations
   2. Symptomatic improvement (e.g., neurological symptom improvement, decreased bone pain)

C. **Hereditary Hemochromatosis**
   Member is experiencing benefit from therapy as evidenced by a decrease in serum ferritin levels as compared to pretreatment baseline.

V. **REFERENCES**
SPECIALTY GUIDELINE MANAGEMENT

TAXOTERE (docetaxel)
DOCEFREZ (docetaxel)
docetaxel (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Breast Cancer
   a. Docetaxel is indicated for the treatment of patients with locally advanced or metastatic breast cancer after failure of prior chemotherapy.
   b. Docetaxel in combination with doxorubicin and cyclophosphamide is indicated for the adjuvant treatment of patients with operable node-positive breast cancer.

2. Non-Small Cell Lung Cancer (NSCLC)
   a. Docetaxel as a single agent is indicated for the treatment of patients with locally advanced or metastatic NSCLC after failure of prior platinum-based chemotherapy.
   b. Docetaxel in combination with cisplatin is indicated for the treatment of patients with unresectable, locally advanced or metastatic NSCLC who have not previously received chemotherapy for this condition.

3. Prostate Cancer
   Docetaxel in combination with prednisone is indicated for the treatment of patients with androgen independent (hormone refractory) metastatic prostate cancer.

4. Gastric Adenocarcinoma
   Docetaxel in combination with cisplatin and fluorouracil is indicated for the treatment of patients with advanced gastric adenocarcinoma, including adenocarcinoma of the gastroesophageal junction, who have not received prior chemotherapy for advanced disease.

5. Head and Neck Cancer
   Docetaxel in combination with cisplatin and fluorouracil (5FU) is indicated for the induction treatment of patients with locally advanced squamous cell carcinoma of the head and neck (SCCHN).

B. Compendial Uses

1. Bladder cancer, primary carcinoma of the urethra, upper genitourinary (GU) tract tumors, urothelial carcinoma of the prostate
2. Bone cancer: Ewing’s sarcoma and osteosarcoma
3. Breast cancer
4. Esophageal and esophagogastric junction cancers
5. Gastric cancer
6. Head and neck cancer
7. Non-small cell lung cancer
8. Occult primary
9. Ovarian cancer: epithelial ovarian cancer, fallopian tube cancer, primary peritoneal cancer, malignant
germ cell tumors, malignant sex cord-stromal tumors, carcinosarcoma - malignant mixed Müllerian
tumors, clear cell carcinoma, mucinous carcinoma, low-grade serious/grade 1 endometrioid epithelial
carcinoma.
10. Prostate cancer
11. Small cell lung cancer
12. Soft tissue sarcoma (STS)
13. Thyroid carcinoma: anaplastic carcinoma
14. Uterine neoplasms: endometrial carcinoma and uterine sarcoma

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Bladder Cancer, Primary Carcinoma of the Urethra, Upper Genitourinary Tract Tumors, Urothelial
carcinoma of the Prostate
   1. Bladder Cancer
      Authorization of 12 months may be granted for treatment of bladder cancer.

   2. Primary Carcinoma of the Urethra, Upper Genitourinary Tract Tumors, or Urothelial Carcinoma
      of the Prostate
      Authorization of 12 months may be granted for treatment of recurrent or metastatic primary carcinoma
      of the urethra, upper genitourinary tract tumors, or urothelial carcinoma of the prostate.

B. Bone Cancer
   1. Ewing’s Sarcoma
      Authorization of 12 months may be granted for treatment of relapsed, progressive or metastatic
      Ewing’s sarcoma.

   2. Osteosarcoma
      Authorization of 12 months may be granted for treatment of relapsed/refractory or metastatic
      osteosarcoma.

C. Breast Cancer
   Authorization of 12 months may be granted for treatment of breast cancer.

D. Esophageal and Esophagogastric Junction Cancers
   Authorization of 12 months may be granted for treatment of esophageal or esophagogastric junction
   cancer.

E. Gastric Cancer
   Authorization of 12 months may be granted for treatment of gastric cancer.

F. Head and Neck Cancer
   Authorization of 12 months may granted for treatment of head and neck cancer.

G. Non-Small Cell Lung Cancer (NSCLC)
   Authorization of 12 months may be granted for treatment of non-small cell lung cancer.
H. **Occult Primary**  
Authorization of 12 months may be granted for treatment of occult primary cancer.

I. **Ovarian Cancer**  
1. **Epithelial Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer**  
Authorization of 12 months may be granted for treatment of epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer.

2. **Malignant Germ Cell Tumors**  
Authorization of 12 months may be granted for treatment of malignant germ cell tumors.

3. **Malignant Sex-Cord Stromal Tumors**  
Authorization of 12 months may be granted for treatment of malignant sex-cord stromal tumors.

4. **Carcinosarcoma (Malignant Mixed Müllerian Tumors)**  
Authorization of 12 months may be granted for treatment of malignant mixed Müllerian tumors.

5. **Clear Cell Carcinoma**  
Authorization of 12 months may be granted for treatment of clear cell carcinoma.

6. **Mucinous Carcinoma**  
Authorization of 12 months may be granted for treatment of mucinous carcinoma.

7. **Low-Grade Serous/Grade 1 Endometrioid Epithelial Carcinoma**  
Authorization of 12 months may be granted for treatment of low-grade serous/grade 1 endometrioid epithelial carcinoma.

J. **Prostate Cancer**  
Authorization of 12 months may be granted for treatment of prostate cancer.

K. **Small Cell Lung Cancer (SCLC)**  
Authorization of 12 months may be granted for treatment of small cell lung cancer.

L. **Soft Tissue Sarcoma (STS)**  
Authorization of 12 months may be granted for treatment of soft tissue sarcoma.

M. **Thyroid Carcinoma – Anaplastic Carcinoma**  
Authorization of 12 months may be granted for treatment of thyroid carcinoma-anaplastic carcinoma.

N. **Uterine Neoplasms**  
1. **Endometrial Carcinoma**  
Authorization of 12 months may be granted for treatment of endometrial carcinoma.

2. **Uterine Sarcoma**  
Authorization for 12 months may be granted for treatment of uterine sarcoma.

III. **CONTINUATION OF THERAPY**

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.
IV. DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

TIKOSYN (dofetilide)
dofetilide (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Maintenance of normal sinus rhythm (delay in time to recurrence of atrial flutter/atrial fibrillation [AF/AFI]) in patients with AF/AFI of greater than one week duration who have been converted to normal sinus rhythm
   2. Conversion of AF/AFI to normal sinus rhythm

B. Compendial Uses
   1. Supraventricular tachycardia
   2. Ventricular tachyarrhythmia

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR APPROVAL

1. Atrial Flutter/Atrial fibrillation
   Authorization of 12 months may be granted for the maintenance of, or conversion to, normal sinus rhythm after atrial flutter or atrial fibrillation.

2. Supraventricular tachycardia
   Authorization of 12 months may be granted for the treatment and prevention of supraventricular tachycardia.

3. Ventricular tachyarrhythmia
   Authorization of 12 months may be granted for the treatment and prevention of ventricular tachyarrhythmia.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria.

IV. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

DUPIXENT (dupilumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
A. Dupixent is indicated for the treatment of patients aged 12 years and older with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Dupixent can be used with or without topical corticosteroids.
B. Dupixent is indicated as an add-on maintenance treatment in patients with moderate-to-severe asthma aged 12 years and older with an eosinophilic phenotype or with oral corticosteroid dependent asthma.
C. Dupixent is indicated as an add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with nasal polyposis (CRSwNP).

Limitation of Use: Dupixent is not indicated for the relief of acute bronchospasm or status asthmaticus

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Atopic dermatitis (for initial requests): Member’s chart or medical record showing prerequisite therapies (see section III.A.2).
B. Asthma (for initial requests): Member’s chart or medical record showing pretreatment blood eosinophil count and if applicable, oral glucocorticoid use history, including drug, dose, frequency and duration.
C. Chronic rhinosinusitis with nasal polyposis (for initial requests): Member’s chart or medical record showing nasal endoscopy or anterior rhinoscopy details (e.g., location, size).

III. CRITERIA FOR INITIAL APPROVAL

A. Moderate-to-severe atopic dermatitis
Authorization of 4 months may be granted for treatment of moderate-to-severe atopic dermatitis in members 12 years of age or older when all of the following criteria is met:
1. Affected body surface is greater than or equal to 10% body surface area OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
2. Member has had an inadequate treatment response to a high potency topical corticosteroid (see Appendix) or a topical calcineurin inhibitor in the past 180 days, or the use of topical corticosteroids and topical calcineurin inhibitors is not advisable for the member (e.g., due to contraindications or prior intolerances).
B. Asthma

Authorization of 6 months may be granted for treatment of asthma in members 12 years of age or older when all of the following criteria are met:

1. Member meets one of the following criteria:
   a. Member has inadequate asthma control (e.g., hospitalization or emergency medical care visit within the past year) despite current treatment with all of the following medications at optimized doses*:
      i. High-dose inhaled corticosteroid
      ii. Additional controller (long acting beta2-agonist, leukotriene modifier, or sustained-release theophylline)
      iii. Oral glucocorticoids (at least 5 mg per day of prednisone/prednisolone or equivalent)
   *Members should be receiving treatment with inhaled corticosteroid and additional controller for at least the previous 3 months, and oral glucocorticoids for most days during the previous 6 months (e.g., 50% of days, 3 steroid bursts in the previous 6 months).
   b. Member has a baseline blood eosinophil count of at least 150 cells per microliter and inadequate asthma control (e.g., hospitalization or emergency medical care visit within the past year) despite current treatment with both of the following medications at optimized doses:
      i. Inhaled corticosteroid
      ii. Additional controller (long acting beta2-agonist, leukotriene modifier, or sustained-release theophylline)

2. Member will not use Dupixent as monotherapy
3. Member does not currently smoke.
4. Member will not use Dupixent concomitantly with other biologics (e.g., Cinqair, Fasenra, Nucala or Xolair).

C. Chronic rhinosinusitis with nasal polyposis (CRSwNP)

Authorization of 6 months may be granted for treatment of CRSwNP in members 18 years of age or older when all of the following criteria are met:

1. Member has bilateral nasal polyposis and chronic symptoms of sinusitis despite intranasal corticosteroid treatment for at least 2 months unless contraindicated or not tolerated; and
2. The member has CRSwNP despite one of the following:
   a. Prior sino-nasal surgery; or
   b. Prior treatment with systemic corticosteroids within the last two years was ineffective, unless contraindicated or not tolerated; and
3. Member has a bilateral nasal endoscopy or anterior rhinoscopy showing polyps reaching below the lower border of the middle turbinate or beyond in each nostril; and
4. Member has nasal obstruction plus one additional symptom:
   a. Rhinorrhea (anterior/posterior); or
   b. Reduction or loss of smell; and
5. Member will be using a daily intranasal corticosteroid while being treated with Dupixent, unless contraindicated or not tolerated.

IV. CONTINUATION OF THERAPY

A. Moderate-to-severe atopic dermatitis

Authorization of 12 months may be granted for members 12 years of age or older who achieve or maintain positive clinical response with Dupixent therapy for moderate-to-severe atopic dermatitis as evidenced by low disease activity (i.e., clear or almost clear skin), or improvement in signs and symptoms of atopic dermatitis (e.g., redness, itching, oozing/crusting).

B. Asthma
Authorization of 12 months may be granted for members 12 years of age or older when all of the following criteria are met:

1. Asthma control has improved on Dupixent treatment as demonstrated by at least one of the following:
   a. A reduction in the frequency and/or severity of symptoms and exacerbations
   b. A reduction in the daily maintenance oral corticosteroid dose
2. Member will not use Dupixent as monotherapy
3. Member does not currently smoke.
4. Member will not use Dupixent concomitantly with other biologics (e.g., Cinqair, Fasenra, Nucala or Xolair)

C. Chronic rhinosinusitis with nasal polyposis (CRSwNP)
   Authorization of 12 months may be granted for members 18 years of age or older who achieve or maintain positive clinical response to Dupixent therapy as evidenced by improvement in signs and symptoms of CRSwNP (e.g., improvement in nasal congestion, nasal polyp size, loss of smell, anterior or posterior rhinorrhea, sinonasal inflammation, hyposmia and/or facial pressure or pain or reduction in corticosteroid use).

APPENDIX: Relative potency of select topical corticosteroid products

<table>
<thead>
<tr>
<th>Potency</th>
<th>Drug</th>
<th>Dosage form</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Very high potency</td>
<td>Augmented betamethasone dipropionate</td>
<td>Ointment, Gel, Cream, Ointment</td>
<td>0.05%</td>
</tr>
<tr>
<td></td>
<td>Clobetasol propionate</td>
<td></td>
<td>0.05%</td>
</tr>
<tr>
<td></td>
<td>Diflorasone diacetate</td>
<td>Ointment</td>
<td>0.05%</td>
</tr>
<tr>
<td></td>
<td>Halobetasol propionate</td>
<td>Cream, Ointment</td>
<td>0.05%</td>
</tr>
<tr>
<td>Potency</td>
<td>Drug</td>
<td>Dosage form</td>
<td>Strength</td>
</tr>
<tr>
<td>----------</td>
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</tr>
<tr>
<td></td>
<td>Amcinonide</td>
<td>Cream, Lotion, Ointment</td>
<td>0.1%</td>
</tr>
<tr>
<td></td>
<td>Augmented betamethasone dipropionate</td>
<td>Cream, Lotion</td>
<td>0.05%</td>
</tr>
<tr>
<td></td>
<td>Betamethasone dipropionate</td>
<td>Cream, Ointment</td>
<td>0.05%</td>
</tr>
<tr>
<td></td>
<td>Betamethasone valerate</td>
<td>Ointment</td>
<td>0.1%</td>
</tr>
<tr>
<td></td>
<td>Desoximetasone</td>
<td>Cream, Ointment, Gel</td>
<td>0.25%</td>
</tr>
<tr>
<td></td>
<td>Diflorasone diacetate</td>
<td>Cream, Ointment (emollient base)</td>
<td>0.05%</td>
</tr>
<tr>
<td></td>
<td>Fluocinonide</td>
<td>Cream, Ointment, Gel</td>
<td>0.05%</td>
</tr>
<tr>
<td></td>
<td>Halcinonide</td>
<td>Cream, Ointment</td>
<td>0.1%</td>
</tr>
<tr>
<td>II. High potency</td>
<td>Triamcinolone acetonide</td>
<td>Cream, Ointment</td>
<td>0.5%</td>
</tr>
<tr>
<td></td>
<td>Betamethasone dipropionate</td>
<td>Lotion</td>
<td>0.05%</td>
</tr>
<tr>
<td></td>
<td>Betamethasone valerate</td>
<td>Cream</td>
<td>0.1%</td>
</tr>
<tr>
<td></td>
<td>Clocortolone pivalate</td>
<td>Cream</td>
<td>0.1%</td>
</tr>
<tr>
<td></td>
<td>Desoximetasone</td>
<td>Cream</td>
<td>0.05%</td>
</tr>
<tr>
<td></td>
<td>Fluocinolone acetonide</td>
<td>Cream, Ointment</td>
<td>0.025%</td>
</tr>
<tr>
<td></td>
<td>Flurandrenolide</td>
<td>Cream, Ointment, Lotion</td>
<td>0.05%</td>
</tr>
<tr>
<td></td>
<td>Fluticasone propionate</td>
<td>Tape, 4 mcg/cm²</td>
<td></td>
</tr>
<tr>
<td>III. Medium potency</td>
<td>Hydrocortisone butyrate</td>
<td>Ointment, Solution</td>
<td>0.1%</td>
</tr>
<tr>
<td></td>
<td>Hydrocortisone valerate</td>
<td>Cream, Ointment</td>
<td>0.2%</td>
</tr>
<tr>
<td></td>
<td>Mometasone furoate</td>
<td>Cream, Ointment, Lotion</td>
<td>0.1%</td>
</tr>
<tr>
<td></td>
<td>Prednicarbate</td>
<td>Cream, Ointment</td>
<td>0.1%</td>
</tr>
<tr>
<td></td>
<td>Triamcinolone acetonide</td>
<td>Cream, Ointment, Lotion</td>
<td>0.025%, 0.1%</td>
</tr>
<tr>
<td></td>
<td>Alclometasone dipropionate</td>
<td>Cream, Ointment</td>
<td>0.05%</td>
</tr>
<tr>
<td></td>
<td>Desonide</td>
<td>Cream</td>
<td>0.05%</td>
</tr>
<tr>
<td></td>
<td>Fluocinolone acetonide</td>
<td>Cream, Solution</td>
<td>0.01%</td>
</tr>
<tr>
<td></td>
<td>Hydrocortisone</td>
<td>Lotion</td>
<td>0.25%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cream, Ointment, Lotion, Aerosol</td>
<td>0.5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cream, Ointment, Lotion, Solution</td>
<td>1%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cream, Ointment, Lotion</td>
<td>2.5%</td>
</tr>
<tr>
<td>IV. Low potency</td>
<td>Hydrocortisone acetate</td>
<td>Cream, Ointment</td>
<td>0.5%, 1%</td>
</tr>
</tbody>
</table>

V. REFERENCES
ENHANCED SPECIALTY GUIDELINE MANAGEMENT

DUPIXENT (dupilumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
A. Dupixent is indicated for the treatment of patients aged 12 years and older with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Dupixent can be used with or without topical corticosteroids.
B. Dupixent is indicated as an add-on maintenance treatment in patients with moderate-to-severe asthma aged 12 years and older with an eosinophilic phenotype or with oral corticosteroid dependent asthma.
C. Dupixent is indicated as an add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with nasal polyposis (CRSwNP).

Limitation of Use: Dupixent is not indicated for the relief of acute bronchospasm or status asthmaticus

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Atopic dermatitis (initial requests): Member’s chart or medical record showing prerequisite therapies and affected area(s) and body surface area (see section IV.A.1).
B. Asthma (initial requests): Member’s chart or medical record showing pretreatment blood eosinophil count and prerequisite therapies. For oral glucocorticoid use history, the documentation must also include drug, dose, frequency and duration.
C. Chronic rhinosinusitis with nasal polyposis (for initial requests): Member’s chart or medical record showing nasal endoscopy or anterior rhinoscopy details (e.g., location, size).

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with one of the following:
A. Atopic dermatitis: dermatologist or allergist/immunologist
B. Asthma: allergist/immunologist or pulmonologist
C. Chronic rhinosinusitis with nasal polyposis: allergist/immunologist or otolaryngologist

IV. CRITERIA FOR INITIAL APPROVAL
A. **Moderate-to-severe atopic dermatitis**

Authorization of 4 months may be granted for treatment of moderate-to-severe atopic dermatitis in members 12 years of age or older when all of the following criteria are met:

1. Affected body surface area is greater than or equal to 10% OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
2. Member has had an inadequate treatment response to topical tacrolimus (Protopic) and at least two medium or higher potency topical corticosteroids in the past 180 days, OR topical corticosteroids or topical tacrolimus are not advisable for the member.

B. **Moderate-to-severe asthma**

Authorization of 6 months may be granted for treatment of moderate-to-severe asthma in members 12 years of age or older when all of the following criteria are met:

1. Member meets one of the following criteria:
   a. Member has inadequate asthma control (e.g. hospitalization or emergency medical care visit within the past year) despite current treatment with all of the following medications at optimized doses*:
      i. High-dose inhaled corticosteroid
      ii. Additional controller (long acting beta-agonist, leukotriene modifier, or sustained-release theophylline)
      iii. Oral glucocorticoids (at least 5 mg per day of prednisone/prednisolone or equivalent)
   *Members should be receiving treatment with inhaled corticosteroid and additional controller for at least the previous 3 months, and oral glucocorticoids for most days during the previous 6 months (e.g. 50% of days, 3 steroid bursts in the previous 6 months).
   b. Member has a baseline blood eosinophil count of at least 150 cells per microliter and asthma is inadequately controlled despite treatment for at least 3 months with both of the following at optimized doses:
      i. Medium-to-high-dose inhaled corticosteroid
      ii. Additional controller (long acting beta2-agonist, leukotriene modifier, or sustained-release theophylline)
2. Member will not use Dupixent as monotherapy
3. Member does not currently smoke
4. Member will not use Dupixent concomitantly with other biologics (e.g., Cinqair, Fasenra, Nucala or Xolair).

C. **Chronic rhinosinusitis with nasal polyposis (CRSwNP)**

Authorization of 6 months may be granted for treatment of CRSwNP in members 18 years of age or older when all of the following criteria are met:

1. Member has bilateral nasal polyposis and chronic symptoms of sinusitis despite intranasal corticosteroid treatment for at least 2 months unless contraindicated or not tolerated; and
2. The member has CRSwNP despite one of the following:
   a. Prior sino-nasal surgery; or
   b. Prior treatment with systemic corticosteroids within the last two years was ineffective, unless contraindicated or not tolerated; and
3. Member has a bilateral nasal endoscopy or anterior rhinoscopy showing polyps reaching below the lower border of the middle turbinate or beyond in each nostril; and
4. Member has nasal obstruction plus one additional symptom:
   a. Rhinorrhea (anterior/posterior); or
   b. Reduction or loss of smell; and
5. Member will be using a daily intranasal corticosteroid while being treated with Dupixent, unless contraindicated or not tolerated.
V. CONTINUATION OF THERAPY

A. Moderate-to-severe atopic dermatitis
Authorization of 6 months may be granted for members 12 years of age or older who achieve or maintain positive clinical response with Dupixent therapy for moderate-to-severe atopic dermatitis as evidenced by low disease activity (i.e., clear or almost clear skin) or improvement in signs and symptoms of atopic dermatitis (e.g., redness, itching, oozing/crusting).

B. Moderate-to-severe asthma
Authorization of 12 months may be granted for members 12 years of age or older when all of the following criteria are met:
1. Member has achieved and maintained positive clinical response with Dupixent therapy for asthma as evidenced by at least one of the following:
   a. A reduction in the frequency and/or severity of symptoms and exacerbations
   b. A reduction in the daily maintenance oral corticosteroid dose
2. Member will not use Dupixent as monotherapy
3. Member does not currently smoke.
4. Member will not use Dupixent concomitantly with other biologics (e.g., Cinqair, Fasenra, Nucala or Xolair)

C. Chronic rhinosinusitis with nasal polyposis (CRSwNP)
Authorization of 12 months may be granted for members 18 years of age or older who achieve or maintain positive clinical response to Dupixent therapy as evidenced by improvement in signs and symptoms of CRSwNP (e.g., improvement in nasal congestion, nasal polyp size, loss of smell, anterior or posterior rhinorhea, sinonasal inflammation, hyposmia and/or facial pressure or pain or reduction in corticosteroid use).

VI. APPENDIX: Relative potency of select topical corticosteroid products

<table>
<thead>
<tr>
<th>Potency</th>
<th>Drug</th>
<th>Dosage form</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Very high potency</td>
<td>Augmented betamethasone dipropionate</td>
<td>Ointment, Gel</td>
<td>0.05%</td>
</tr>
<tr>
<td></td>
<td>Clobetasol propionate</td>
<td>Cream, Ointment</td>
<td>0.05%</td>
</tr>
<tr>
<td></td>
<td>Diflorasone diacetate</td>
<td>Ointment</td>
<td>0.05%</td>
</tr>
<tr>
<td></td>
<td>Halobetasol propionate</td>
<td>Cream, Ointment</td>
<td>0.05%</td>
</tr>
<tr>
<td></td>
<td>Amcinonide</td>
<td>Cream, Lotion, Ointment</td>
<td>0.1%</td>
</tr>
<tr>
<td></td>
<td>Augmented betamethasone dipropionate</td>
<td>Cream, Lotion</td>
<td>0.05%</td>
</tr>
<tr>
<td></td>
<td>Betamethasone dipropionate</td>
<td>Cream, Ointment</td>
<td>0.05%</td>
</tr>
<tr>
<td></td>
<td>Betamethasone valerate</td>
<td>Ointment</td>
<td>0.1%</td>
</tr>
<tr>
<td></td>
<td>Desoximetasone</td>
<td>Cream, Ointment</td>
<td>0.25%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gel</td>
<td>0.05%</td>
</tr>
<tr>
<td></td>
<td>Diflorasone diacetate</td>
<td>Cream, Ointment (emollient base)</td>
<td>0.05%</td>
</tr>
<tr>
<td></td>
<td>Fluocinonide</td>
<td>Cream, Ointment, Gel</td>
<td>0.05%</td>
</tr>
<tr>
<td></td>
<td>Halcinonide</td>
<td>Cream, Ointment</td>
<td>0.1%</td>
</tr>
<tr>
<td></td>
<td>Triamcinolone acetonide</td>
<td>Cream, Ointment</td>
<td>0.5%</td>
</tr>
<tr>
<td></td>
<td>Betamethasone dipropionate</td>
<td>Lotion</td>
<td>0.05%</td>
</tr>
</tbody>
</table>
### Potency

#### III. Medium potency

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage form</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>Betamethasone valerate</td>
<td>Cream</td>
<td>0.1%</td>
</tr>
<tr>
<td>Clocortolone pivalate</td>
<td>Cream</td>
<td>0.1%</td>
</tr>
<tr>
<td>Desoximetasone</td>
<td>Cream</td>
<td>0.05%</td>
</tr>
<tr>
<td>Fluocinolone acetonide</td>
<td>Cream, Ointment</td>
<td>0.025%</td>
</tr>
<tr>
<td>Flurandrenolide</td>
<td>Cream, Ointment, Lotion</td>
<td>0.05%</td>
</tr>
<tr>
<td>Fluticasone propionate</td>
<td>Cream</td>
<td>0.05%</td>
</tr>
<tr>
<td>Hydrocortisone butyrate</td>
<td>Ointment, Solution</td>
<td>0.1%</td>
</tr>
<tr>
<td>Hydrocortisone valerate</td>
<td>Cream, Ointment</td>
<td>0.2%</td>
</tr>
<tr>
<td>Mometasone furoate</td>
<td>Cream, Ointment, Lotion</td>
<td>0.1%</td>
</tr>
<tr>
<td>Prednicarbate</td>
<td>Cream, Ointment</td>
<td>0.1%</td>
</tr>
<tr>
<td>Triamcinolone acetonide</td>
<td>Cream, Ointment, Lotion</td>
<td>0.025%, 0.1%</td>
</tr>
</tbody>
</table>

#### IV. Low potency

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage form</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alclometasone dipropionate</td>
<td>Cream, Ointment</td>
<td>0.05%</td>
</tr>
<tr>
<td>Desonide</td>
<td>Cream</td>
<td>0.05%</td>
</tr>
<tr>
<td>Fluocinolone acetonide</td>
<td>Cream, Solution</td>
<td>0.01%</td>
</tr>
<tr>
<td>Hydrocortisone</td>
<td>Lotion, Cream, Ointment, Lotion, Solution Aerosol</td>
<td>0.25%, 0.5%, 1%, 2.5%</td>
</tr>
<tr>
<td>Hydrocortisone acetate</td>
<td>Cream, Ointment</td>
<td>0.5%, 1%</td>
</tr>
</tbody>
</table>

### VII. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

DYSPORT (abobotulinumtoxin A)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Treatment of cervical dystonia in adults
   2. Treatment of spasticity (upper and/or lower limb) in adults
   3. Treatment of lower limb spasticity in pediatric patients 2 years of age and older

B. Compendial Uses
   Treatment of benign essential blepharospasm

All other indications are considered experimental/investigational and are not a covered benefit.

II. EXCLUSIONS

Coverage will not be provided for cosmetic use.

III. CRITERIA FOR INITIAL APPROVAL

A. Cervical dystonia
   Authorization of 24 months may be granted for treatment of cervical dystonia (e.g., torticollis).

B. Upper limb spasticity
   Authorization of 24 months may be granted for treatment of upper limb spasticity.

C. Lower limb spasticity
   Authorization of 24 months may be granted for treatment of lower limb spasticity (e.g., cerebral palsy, multiple sclerosis).

D. Blepharospasm
   Authorization of 24 months may be granted for treatment of benign essential blepharospasm.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.
V. REFERENCES

## PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>ALPROSTADILS</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRAND NAME*</td>
<td>CAVERJECT (alprostadil)</td>
</tr>
<tr>
<td></td>
<td>EDEX (alprostadil)</td>
</tr>
<tr>
<td></td>
<td>MUSE (alprostadil)</td>
</tr>
</tbody>
</table>

*Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

### FDA-APPROVED INDICATIONS

**Caverject**
Caverject is indicated for the treatment of erectile dysfunction.
Caverject is also indicated as an adjunct to other diagnostic tests in the diagnosis of erectile dysfunction.

**Edex**
Edex is indicated for the treatment of erectile dysfunction due to neurogenic, vasculogenic, psychogenic, or mixed etiology.

**MUSE**
MUSE is indicated for the treatment of erectile dysfunction. Studies that established benefit demonstrated improvements in success rates for sexual intercourse compared with similarly administered placebo.

### COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for erectile dysfunction in a patient that is 18 years of age or older

Quantity Limits apply.

### RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Caverject, Edex, and MUSE are indicated for the treatment of erectile dysfunction. These drugs are not indicated for use in newborns or children.1-6

According to the American Urological Association (AUA) Guideline on the Management of Erectile Dysfunction, patients presenting with symptoms of erectile dysfunction (ED) should undergo a thorough medical, sexual, and psychosocial history; a physical examination; and selective laboratory testing. Shared decision-making is the cornerstone of patient-centered care for ED. Determining an appropriate treatment requires that the patient, his clinician, and ideally the partner navigate all of these issues in order to arrive at a treatment choice that is aligned with the patient and the partner’s priorities and values. Patients should be informed of all treatment options that are not medically contraindicated and
supported in the shared decision-making process to determine the appropriate treatment.\textsuperscript{7} The dose of alprostadil should be individualized for each patient by careful titration under supervision by the physician.\textsuperscript{1,6}

Since Caverject, Edex, and MUSE are used as needed, the quantity limit for these drugs are based upon coital frequency from studies of data analysis. According to the Predictors of Adult Sexual Activity in The United States survey, men and women between the ages of 25 and 45 have sex a mean 5.7 and 6.4 times per month, respectively.\textsuperscript{6} A Study of Sexuality and Health among Older Adults in the United States found that the prevalence of sexual activity declined with age and that 54% of sexually active persons age 75-85 reported having sex at least two to three times per month.\textsuperscript{9} Therefore, the quantity for approval for alprostadil will be 6 units per month.

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases, the filling limit and day supply may be less than what is indicated.

REFERENCES

CRITERIA FOR APPROVAL

1. Is the requested drug being prescribed for erectile dysfunction in a patient that is 18 years of age or older? Yes No

2. Does the patient require MORE than the plan allowance of 6 units per month of the requested drug? Yes No

[RPh Note: If yes, then deny and enter a partial approval for 6 units per month of the requested drug.]
### Guidelines for Approval

<table>
<thead>
<tr>
<th>Duration of Approval</th>
<th>36 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quantity for Approval</td>
<td>6 units per 25 days*</td>
</tr>
<tr>
<td></td>
<td>18 units per 75 days*</td>
</tr>
</tbody>
</table>

**Set 1**

<table>
<thead>
<tr>
<th>Yes to question(s)</th>
<th>No to question(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

*The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

### Mapping Instructions

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
<th>DENIAL REASONS – DO NOT USE FOR MEDICARE PART D</th>
</tr>
</thead>
</table>
| 1.  | Go to 2 | Deny You do not meet the requirements of your plan.  
Your plan covers this drug when you meet all of these conditions:  
- You are 18 years of age or older  
- You have erectile dysfunction  
Your request has been denied based on the information we have.  
[Short Description: No approvable diagnosis.] |
| 2.  | Deny | Approve for 36 months (6 units/25 days* or 18 units/75 days*) You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 6 units per month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied.  
[Short Description: Over max quantity.] |

*The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*
# QUANTITY LIMIT CRITERIA

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>ERECTILE DYSFUNCTION - BPH DRUGS</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRAND NAME* (generic)</td>
<td>ALPROSTADILS:</td>
</tr>
<tr>
<td></td>
<td>CAVERJECT (alprostadil)</td>
</tr>
<tr>
<td></td>
<td>EDEX (alprostadil)</td>
</tr>
<tr>
<td></td>
<td>MUSE (alprostadil)</td>
</tr>
<tr>
<td>PHOSPHODIESTERASE TYPE 5 (PDE-5) INHIBITORS:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CIALIS (tadalafil)</td>
</tr>
<tr>
<td></td>
<td>LEVITRA (vardenafil hydrochloride)</td>
</tr>
<tr>
<td></td>
<td>STAXYN (vardenafil hydrochloride orally disintegrating)</td>
</tr>
<tr>
<td></td>
<td>STENDRA (avanafil)</td>
</tr>
<tr>
<td></td>
<td>VIAGRA (sildenafil)</td>
</tr>
</tbody>
</table>

*Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*
FDA-APPROVED INDICATION

Alprostadils

Caverject
Caverject is indicated for the treatment of erectile dysfunction.
Caverject is also indicated as an adjunct to other diagnostic tests in the diagnosis of erectile dysfunction.

Edex
Edex is indicated for the treatment of erectile dysfunction due to neurogenic, vasculogenic, psychogenic, or mixed etiology.

MUSE
MUSE is indicated for the treatment of erectile dysfunction. Studies that established benefit demonstrated improvements in success rates for sexual intercourse compared with similarly administered placebo.

Phosphodiesterase type 5 (PDE-5) Inhibitors

Cialis
Erectile Dysfunction
Cialis is indicated for the treatment of erectile dysfunction (ED).
Benign Prostatic Hyperplasia
Cialis is indicated for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH).
Erectile Dysfunction and Benign Prostatic Hyperplasia
Cialis is indicated for the treatment of ED and the signs and symptoms of BPH (ED/BPH).

Limitation of Use
If Cialis is used with finasteride to initiate BPH treatment, such use is recommended for up to 26 weeks because the incremental benefit of Cialis decreases from 4 weeks until 26 weeks, and the incremental benefit of Cialis beyond 26 weeks is unknown.

Levitra
Levitra is indicated for the treatment of erectile dysfunction.

Staxyn
Staxyn is indicated for the treatment of erectile dysfunction.

Stendra
Stendra is a phosphodiesterase 5 (PDE5) inhibitor indicated for the treatment of erectile dysfunction.

Viagra
Viagra is indicated for the treatment of erectile dysfunction.

RATIONALE

Alprostadil and Phosphodiesterase type 5 (PDE-5) Inhibitors [Caverject (alprostadil), Edex (alprostadil), MUSE (alprostadil), Cialis (tadalafil), Levitra (vardenafil hydrochloride), Staxyn (vardenafil hydrochloride orally disintegrating), Stendra (avanafil), Viagra (sildenafil)] are indicated for the treatment of erectile dysfunction (ED). Cialis is also indicated for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH), and for the treatment of ED and the signs and symptoms of BPH (ED/BPH).

Since erectile dysfunction drugs are used as needed (excluding Cialis 2.5 mg and 5 mg), the quantity limits are based upon coital frequency from studies of data analysis. According to the Predictors of Adult Sexual Activity in The United States survey, men and women between the ages of 25 and 45 have sex a mean 5.7 and 6.4 times per month,
respectively. A Study of Sexuality and Health among Older Adults in the United States found that the prevalence of sexual activity declined with age and that 54% of sexually active persons age 75-85 reported having sex at least two to three times per month. Therefore, the quantity limit for erectile dysfunction drugs (excluding Cialis 2.5 mg and 5 mg) will be set at 6 units per month.

The recommended starting dose of Cialis for daily use for ED is 2.5 mg taken at approximately the same time every day, without regard to timing of sexual activity. The Cialis dose for once daily use may be increased to 5 mg based on individual efficacy and tolerability. Therefore, the initial quantity limit for Cialis 2.5 mg and 5 mg will be 30 tablets per month for ED for once daily use.

If the patient is requesting more than the initial quantity limit, then the claim will reject with a message indicating that quantity limits are exceeded.

Please note manufacturer package sizes may vary. It is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases, the filling limit and day supply may be less than what is indicated in the Limit Criteria chart.

REFERENCES
LIMIT CRITERIA

Limits should accumulate across all drugs and strengths up to highest quantity listed depending on the order the claims are processed.

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

<table>
<thead>
<tr>
<th>Medication</th>
<th>1 Month Limit*</th>
<th>3 Month Limit*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cialis (tadalafil) 2.5 mg, 5 mg</td>
<td>30 tablets / 25 days</td>
<td>90 tablets / 75 days</td>
</tr>
<tr>
<td>Cialis (tadalafil) 10 mg, 20 mg</td>
<td>6 tablets / 25 days</td>
<td>18 tablets / 75 days</td>
</tr>
<tr>
<td>Levitra (vardenafil HCl)</td>
<td>6 tablets / 25 days</td>
<td>18 tablets / 75 days</td>
</tr>
<tr>
<td>Staxyn (vardenafil HCl orally disintegrating)</td>
<td>6 tablets / 25 days</td>
<td>18 tablets / 75 days</td>
</tr>
<tr>
<td>Stendra (avanafil)</td>
<td>6 tablets / 25 days</td>
<td>18 tablets / 75 days</td>
</tr>
<tr>
<td>Viagra (sildenafil)</td>
<td>6 tablets / 25 days</td>
<td>18 tablets / 75 days</td>
</tr>
<tr>
<td>Caverject (alprostadil)</td>
<td>6 units / 25 days</td>
<td>18 units / 75 days</td>
</tr>
<tr>
<td>Edex (alprostadil)</td>
<td>6 units / 25 days</td>
<td>18 units / 75 days</td>
</tr>
<tr>
<td>MUSE (alprostadil)</td>
<td>6 units / 25 days</td>
<td>18 units / 75 days</td>
</tr>
</tbody>
</table>

* The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.
## PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>PHOSPHODIESTERASE TYPE 5 (PDE-5) INHIBITORS</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRAND NAME* (generic)</td>
<td></td>
</tr>
<tr>
<td>CIALIS (tadalafil)</td>
<td></td>
</tr>
<tr>
<td>LEVITRA (vardenafil hydrochloride)</td>
<td></td>
</tr>
<tr>
<td>STAXYN (vardenafil hydrochloride orally disintegrating)</td>
<td></td>
</tr>
<tr>
<td>STENDRA (avanafil)</td>
<td></td>
</tr>
<tr>
<td>VIAGRA (sildenafil)</td>
<td></td>
</tr>
</tbody>
</table>

*Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

### FDA-APPROVED INDICATIONS

**Cialis**
- **Erectile Dysfunction**
  Cialis is indicated for the treatment of erectile dysfunction (ED).
- **Benign Prostatic Hyperplasia**
  Ciais is indicated for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH).
- **Erectile Dysfunction and Benign Prostatic Hyperplasia**
  Ciais is indicated for the treatment of ED and the signs and symptoms of BPH (ED/BPH).

**Limitation of Use**
If Cialis is used with finasteride to initiate BPH treatment, such use is recommended for up to 26 weeks because the incremental benefit of Cialis decreases from 4 weeks until 26 weeks, and the incremental benefit of Cialis beyond 26 weeks is unknown.

**Levitra**
Levitra is indicated for the treatment of erectile dysfunction.

**Staxyn**
Staxyn is indicated for the treatment of erectile dysfunction.

**Stendra**
Stendra is a phosphodiesterase 5 (PDE5) inhibitor indicated for the treatment of erectile dysfunction.

**Viagra**
Viagra is indicated for the treatment of erectile dysfunction.
COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- Cialis (tadalafil) 2.5 mg or 5 mg is being prescribed for daily use for symptomatic benign prostatic hyperplasia (BPH) with or without erectile dysfunction (ED) in a patient that is 18 years of age or older
  [Note: Examples of signs and symptoms of BPH are incomplete emptying, weak stream, straining, urinary frequency, intermittency, urgency, or acute urinary retention.]

  OR

- The requested drug is being prescribed for erectile dysfunction in a patient that is 18 years of age or older

  Quantity Limits apply.

RATIONALE
The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Phosphodiesterase type 5 (PDE-5) Inhibitors [Cialis (tadalafil), Levitra (vardenafil hydrochloride), Staxyn (vardenafil hydrochloride orally disintegrating), Stendra (avanafil), and Viagra (sildenafil)] are indicated for the treatment of erectile dysfunction (ED). Cialis is also indicated for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH), and for the treatment of ED and the signs and symptoms of BPH (ED/BPH). These drugs are not indicated for use in children.1-7 Since BPH is typically a condition that occurs in older patients, the Criteria for Approval does not specify this information related to the BPH diagnosis. The age must still be specified for a diagnosis of ED.

ED only
According to the American Urological Association (AUA) Guideline on the Management of Erectile Dysfunction, patients presenting with symptoms of erectile dysfunction (ED) should undergo a thorough medical, sexual, and psychosocial history; a physical examination; and selective laboratory testing. Shared decision-making is the cornerstone of patient-centered care for ED. Determining an appropriate treatment requires that the patient, his clinician, and ideally the partner navigate all of these issues in order to arrive at a treatment choice that is aligned with the patient and the partner’s priorities and values. Patients should be informed of all treatment options that are not medically contraindicated and supported in the shared decision-making process to determine the appropriate treatment.8

Since erectile dysfunction drugs are used as needed (excluding Cialis 2.5 mg and 5 mg), the quantity limits for these drugs are based upon coital frequency from studies of data analysis. According to the Predictors of Adult Sexual Activity in The United States survey, men and women between the ages of 25 and 45 have sex a mean 5.7 and 6.4 times per month, respectively.9 A Study of Sexuality and Health among Older Adults in the United States found that the prevalence of sexual activity declined with age and that 54% of sexually active persons aged 75-85 reported having sex at least two to three times per month.10 Therefore, the quantity for approval for erectile dysfunction drugs (excluding Cialis 2.5 mg and 5 mg) will be 6 units per month.

The recommended starting dose of Cialis for daily use for ED is 2.5 mg taken at approximately the same time every day, without regard to timing of sexual activity. The Cialis dose for once daily use may be increased to 5 mg based on individual efficacy and tolerability.1,6,7 Therefore, the quantity for approval for Cialis 2.5 mg and 5 mg will be 30 tablets per month for ED for once daily use.

BPH and ED/BPH
According to the American Urological Association (AUA) BPH guidelines, lower urinary tract symptoms (LUTS) secondary to BPH may include incomplete emptying, weak stream, straining, urinary frequency, intermittency, or urgency. The presence of moderate-to-severe LUTS is also associated with the development of acute urinary retention (AUR) as a symptom of BPH progression. If drug therapy is considered, decisions will be influenced by coexisting overactive bladder symptoms and prostate size or serum PSA levels. Also, the overall benefit and risks of therapy must be considered. Per AUA BPH guidelines, the primary goal of treatment is to alleviate bothersome LUTS that result from prostatic enlargement and on the alteration of disease progression and prevention of complications that can be associated with BPH/LUTS. If treatment is successful, a yearly follow-up should include a repeat of the initial evaluation to detect any changes that have occurred, if symptoms have progressed, or if a complication has developed.11
The recommended dose of Cialis for once daily use for BPH and ED/BPH is 5 mg, taken at approximately the same time every day, without regard to timing of sexual activity. For BPH and ED/BPH a starting dose of 2.5 mg is recommended for creatinine clearance 30 to 50 mL/min. The quantity for approval for Cialis (tadalafil) 2.5 mg and 5 mg will be 30 tablets per month for once daily use for BPH and ED/BPH.

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

REFERENCES

CRITERIA FOR APPROVAL

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Is this request for Cialis (tadalafil) 2.5 mg or 5 mg?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>[If no, then skip to question 4.]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Is Cialis (tadalafil) 2.5 mg or 5 mg being prescribed for daily use for symptomatic benign prostatic hyperplasia (BPH) with or without erectile dysfunction (ED) in a patient that is 18 years of age or older? [Note: Examples of signs and symptoms of BPH are incomplete emptying, weak stream, straining, urinary frequency, intermittency, urgency, or acute urinary retention.]</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>[If no, then skip to question 4.]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
3. Does the patient require MORE than the plan allowance of 1 tablet per day?  
[No further questions.]  
[**RPh Note:** If yes, then deny and enter a partial approval for 30 tablets per month of Cialis 2.5 mg or Cialis 5 mg.]

4. Is the requested drug being prescribed for erectile dysfunction in a patient that is 18 years of age or older?  

5. Does the patient require MORE than the plan allowance of 30 tablets per month of Cialis 2.5 mg, 5 mg OR MORE than the plan allowance of 6 tablets per month of Cialis 10 mg, 20 mg, Levitra, Staxyn, Stendra, or Viagra?  

[**RPh Note:** If yes, then deny and enter a partial approval per Limit Criteria for Erectile Dysfunction Chart.]

---

### Guidelines for Approval

<table>
<thead>
<tr>
<th>Duration of Approval</th>
<th>36 months</th>
</tr>
</thead>
</table>
| Quantity for Approval | Cialis 2.5 mg OR Cialis 5 mg  
30 tablets per 25 days*  
90 tablets per 75 days* |

#### Quantity for Approval

**Set 1**

<table>
<thead>
<tr>
<th>Yes to question(s)</th>
<th>No to question(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

**Set 2**

<table>
<thead>
<tr>
<th>Yes to question(s)</th>
<th>No to question(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>5</td>
</tr>
</tbody>
</table>

*The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.

### Mapping Instructions

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Go to 2</td>
</tr>
<tr>
<td>2.</td>
<td>Go to 3</td>
</tr>
</tbody>
</table>
| 3.  | Deny | Approve for 36 months Cialis 2.5 mg OR Cialis 5 mg  
30 tablets per 25 days*  
90 tablets per 75 days* |

You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 30 tablets per month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied.  

[**Short Description:** Over max quantity.]

<table>
<thead>
<tr>
<th>4.</th>
<th>Go to 5</th>
<th>Deny</th>
</tr>
</thead>
</table>

You do not meet the requirements of your plan. Your plan covers this drug when you meet any of these conditions:  
- You are 18 years of age or older and you have erectile dysfunction  
- You are using Cialis 2.5 mg or Cialis 5 mg, you are 18 years of age or older, and you have benign prostatic hyperplasia (BPH) that is causing symptoms  
Your request has been denied based on the information we have.  

[**Short Description:** No approvable diagnosis.]
5. **Deny**  
RPh Note: For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage  

<table>
<thead>
<tr>
<th>Medication</th>
<th>1 Month Limit*</th>
<th>3 Month Limit*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cialis (tadalafil) 2.5 mg, 5 mg</td>
<td>30 tablets / 25 days</td>
<td>90 tablets / 75 days</td>
</tr>
<tr>
<td>Cialis (tadalafil) 10 mg, 20 mg</td>
<td>6 tablets / 25 days</td>
<td>18 tablets / 75 days</td>
</tr>
<tr>
<td>Levitra (vardenafil HCl)</td>
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<td>18 tablets / 75 days</td>
</tr>
<tr>
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<td>18 tablets / 75 days</td>
</tr>
<tr>
<td>Stendra (avanafil)</td>
<td>6 tablets / 25 days</td>
<td>18 tablets / 75 days</td>
</tr>
<tr>
<td>Viagra (sildenafil)</td>
<td>6 tablets / 25 days</td>
<td>18 tablets / 75 days</td>
</tr>
</tbody>
</table>

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**LIMIT CRITERIA FOR ERECTILE DYSFUNCTION**

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

<table>
<thead>
<tr>
<th>Medication</th>
<th>1 Month Limit*</th>
<th>3 Month Limit*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cialis (tadalafil) 2.5 mg, 5 mg</td>
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<tr>
<td>Cialis (tadalafil) 10 mg, 20 mg</td>
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<td>18 tablets / 75 days</td>
</tr>
<tr>
<td>Levitra (vardenafil HCl)</td>
<td>6 tablets / 25 days</td>
<td>18 tablets / 75 days</td>
</tr>
<tr>
<td>Staxyn (vardenafil HCl orally disintegrating)</td>
<td>6 tablets / 25 days</td>
<td>18 tablets / 75 days</td>
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<tr>
<td>Stendra (avanafil)</td>
<td>6 tablets / 25 days</td>
<td>18 tablets / 75 days</td>
</tr>
<tr>
<td>Viagra (sildenafil)</td>
<td>6 tablets / 25 days</td>
<td>18 tablets / 75 days</td>
</tr>
</tbody>
</table>

* The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.
SPECIALTY GUIDELINE MANAGEMENT

EGRIFTA (tesamorelin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Egrifta is indicated for the reduction of excess abdominal fat in human immunodeficiency virus (HIV)-infected patients with lipodystrophy.

Limitations of Use:
A. Long-term cardiovascular benefit and safety of Egrifta have not been studied.
B. Egrifta is not indicated for weight loss management (weight neutral effect).
C. There are no data to support improved compliance with anti-retroviral therapies in HIV-positive patients taking Egrifta.

All other indications are considered experimental/investigational and are not a covered benefit.

II. EXCLUSIONS

Coverage will not be provided for weight loss.

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with an infectious disease specialist.

IV. CRITERIA FOR INITIAL APPROVAL

Reduction of excess abdominal fat in human immunodeficiency virus (HIV)-infected patients with lipodystrophy

Authorization of 6 months may be granted to members who meet all of the following criteria:
A. The member has HIV infection and lipodystrophy
B. The member is currently receiving anti-retroviral therapy
C. Egrifta is used to reduce excess abdominal fat
V. CONTINUATION OF THERAPY

Reduction of excess abdominal fat in human immunodeficiency virus (HIV)-infected patients with lipodystrophy
Authorization of 6 months may be granted to members who meet ALL the following criteria:
A. The member has HIV infection and lipodystrophy
B. The member is currently receiving anti-retroviral therapy
C. The member has demonstrated a clear clinical improvement from baseline that is supported by waist circumference measurement or CT scan

VI. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

ELAPRASE (idursulfase)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Elaprase is indicated for patients with Hunter syndrome (Mucopolysaccharidosis II, MPS II). Elaprase has been shown to improve walking capacity in patients 5 years and older. In patients 16 months to 5 years of age, no data are available to demonstrate improvement in disease-related symptoms or long term clinical outcome; however, treatment with Elaprase has reduced spleen volume similarly to that of adults and children 5 years of age and older. The safety and efficacy of Elaprase have not been established in pediatric patients less than 16 months of age.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Mucopolysaccharidosis II (MPS II)
Indefinite authorization may be granted for treatment of MPS II when the diagnosis of MPS II was confirmed by enzyme assay demonstrating a deficiency of iduronate 2-sulfatase enzyme activity or by genetic testing.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

ELELYSO (taliglucerase alfa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Elelyso is indicated for the treatment of patients with a confirmed diagnosis of type 1 Gaucher disease.

II. CRITERIA FOR INITIAL APPROVAL

Gaucher disease type 1
Indefinite authorization may be granted for treatment of Gaucher disease type 1 when the diagnosis of Gaucher disease was confirmed by enzyme assay demonstrating a deficiency of beta-glucocerebrosidase (glucosidase) enzyme activity or by genetic testing.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

ELIDEL
(pimecrolimus)

Status: CVS Caremark Criteria  Ref # 759-A
Type: Initial Prior Authorization  Ref # MDC-2 491-A

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS
Elidel is indicated as second-line therapy for the short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis in non-immunocompromised adults and children 2 years of age and older, who have failed to respond adequately to other topical prescription treatments, or when those treatments are not advisable.
Elidel is not indicated for use in children less than 2 years of age.

Compendial/Off label Uses
Psoriasis - on the face, genitals, or skin folds
Atopic Dermatitis for patients under 2 years of age
Vitiligo on the head or neck

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:
- The requested drug is being prescribed for psoriasis on the face, genitals, or skin folds OR vitiligo on the head or neck
OR
- The requested drug is being prescribed for mild to moderate atopic dermatitis (eczema)
  AND
  o The requested drug will be used around the eyes, on the face, genitals, or skin folds
  OR
  o The patient has experienced an inadequate treatment response, intolerance, or contraindication to at least one first line therapy agent (e.g., medium or higher potency topical corticosteroid)
  OR
  o The patient is less than 2 years of age AND unable to use a first line therapy agent (e.g., medium or higher potency topical corticosteroid)

RATIONALE
These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Elidel (pimecrolimus) is indicated as second-line therapy for the short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis in non-immunocompromised adults and children 2 years of age and older, who have failed to respond adequately to other topical prescription treatments, or when those treatments are not advisable.

According to the American Academy of Dermatology Association (AAD) atopic dermatitis (AD) guidelines, Topical Corticosteroids (TCS) are used in the management of AD and are the mainstay of anti-inflammatory therapy (see examples in Table 1). TCS are recommended for AD affected individuals who have failed to respond to good skin care.
and regular use of emollients alone. Topical calcineurin inhibitors (TCI), such as Elidel, are considered second-line therapy. Situations in which TCI may be preferable to topical steroids include recalcitrance to steroids, use on sensitive areas (e.g., face, anogenital, skin folds), steroid-induced atrophy, and long-term uninterrupted topical steroid use. TCI have the benefit of not carrying risk for cutaneous atrophy, with little negative effect on collagen synthesis and skin thickness; therefore, can be used as steroid-sparing agents and long term studies (to 12 months) have shown that they reduce the need for TCS use.4

### TABLE 1: EXAMPLES OF TOPICAL CORTICOSTEROIDS FOR TREATMENT OF ATOPIC DERMATITIS 2,3,4

<table>
<thead>
<tr>
<th>Medium Potency</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>betamethasone dipropionate lotion, spray 0.05%</td>
<td></td>
</tr>
<tr>
<td>betamethasone valerate crm/lotion 0.1%/foam 0.12%</td>
<td></td>
</tr>
<tr>
<td>clocortolone pivalate crm 0.1%</td>
<td></td>
</tr>
<tr>
<td>desonide lotion, ointment 0.05%</td>
<td></td>
</tr>
<tr>
<td>desoximetasone crm 0.05%</td>
<td></td>
</tr>
<tr>
<td>fluocinolone acetonide crm/ointment 0.025%</td>
<td></td>
</tr>
<tr>
<td>flurandrenolide crm/ointment 0.05%</td>
<td></td>
</tr>
<tr>
<td>fluticasone propionate crm/ointment 0.05%/oint 0.005%</td>
<td></td>
</tr>
<tr>
<td>hydrocortisone butyrate cream/lopcream/ointment/oint/solution 0.1%</td>
<td></td>
</tr>
<tr>
<td>hydrocortisone probutate crm 0.1%</td>
<td></td>
</tr>
<tr>
<td>hydrocortisone valerate crm/oointment 0.2%</td>
<td></td>
</tr>
<tr>
<td>mometasone furoate crm/ointment/solution 0.1%</td>
<td></td>
</tr>
<tr>
<td>prednicarbate crm/oointment 0.1%</td>
<td></td>
</tr>
<tr>
<td>triamcinolone acetonide crm/oointment/kit 0.1%</td>
<td></td>
</tr>
<tr>
<td>triamcinolone acetonide crm/oointment 0.025%</td>
<td></td>
</tr>
<tr>
<td>triamcinolone acetonide ointment 0.05%</td>
<td></td>
</tr>
<tr>
<td>High Potency</td>
<td></td>
</tr>
<tr>
<td>amcinonide crm/oointment 0.1%</td>
<td></td>
</tr>
<tr>
<td>betamethasone dipropionate crm/oointment 0.05%</td>
<td></td>
</tr>
<tr>
<td>betamethasone dipropionate augmented crm/oointment 0.05%</td>
<td></td>
</tr>
<tr>
<td>betamethasone valerate oint 0.1%</td>
<td></td>
</tr>
<tr>
<td>desoximetasone crm/oointment 0.25%/gel/oointment 0.05%</td>
<td></td>
</tr>
<tr>
<td>diflorasone diacetate crm (emollient base) 0.05%</td>
<td></td>
</tr>
<tr>
<td>halcinonide crm/oointment 0.1%</td>
<td></td>
</tr>
<tr>
<td>fluocinolone crm/emulsified cream/oointment/gel/solution 0.05%</td>
<td></td>
</tr>
<tr>
<td>mometasone furoate oint 0.1%</td>
<td></td>
</tr>
<tr>
<td>triamcinolone acetonide crm/oointment 0.5%</td>
<td></td>
</tr>
<tr>
<td>triamcinolone acetonide aerosol solution 0.147 mg/g</td>
<td></td>
</tr>
<tr>
<td>Very High Potency</td>
<td></td>
</tr>
<tr>
<td>betamethasone dipropionate augmented oint/gel 0.05%</td>
<td></td>
</tr>
<tr>
<td>clobetasol propionate crm/oointment/shampoo/gel/ointment/solution/spray 0.05%/cream 0.025%</td>
<td></td>
</tr>
<tr>
<td>diflorasone diacetate oint 0.05%</td>
<td></td>
</tr>
<tr>
<td>flurandrenolide tape 4mcg/cm²</td>
<td></td>
</tr>
<tr>
<td>halobetasol propionate crm/oointment/kit 0.05%</td>
<td></td>
</tr>
<tr>
<td>fluocinonide crm 0.1%</td>
<td></td>
</tr>
</tbody>
</table>

The AAD guidelines indicate that children have a proportionately greater body surface area to weight ratio, and as a result, have a higher degree of absorption for the same amount applied. But during significant acute flares, the use of mid- or higher-potency TCS for short courses may be appropriate to gain rapid control of symptoms, even in children. For patients less than 2 years of age with AD, off label use of 0.03% tacrolimus or 1% pimecrolimus can be recommended. Evidence from clinical trials supports the safe and effective use of topical tacrolimus 0.03% and pimecrolimus in children younger than 2 years, including in infants.4 In a 5-year open label study (‘Petite’), 2418 infants with AD were randomized to pimecrolimus 1% with short term topical corticosteroids for flares or topical corticosteroids (low potency, e.g., hydrocortisone 1%; or medium potency, e.g., hydrocortisone butyrate 0.1%). Both pimecrolimus and topical corticosteroids had a rapid onset of action with greater than 50% of patients achieving treatment success by week 3. After 5 years, greater than 85% and 95% of patients in each group achieved overall and facial treatment success, respectively. The pimecrolimus group required substantially fewer steroid days than the topical corticosteroid group (7 v 178). The profile and frequency of adverse events was similar in the 2 groups; in both groups, there was no evidence for impairment of humoral or cell immunity. The study concluded that long-term management of mild to moderate AD in infants with pimecrolimus or TCS was safe without any effect on the immune system. Pimecrolimus was steroid-sparing. The data suggest pimecrolimus had similar efficacy to TCS and support the use of pimecrolimus as a first-line treatment.
of mild to moderate AD in infants and children. However, Elidel is not indicated for the use in children less than 2 years of age and long term safety and effects on the developing immune system are unknown. Two phase 3 trials involving 436 infants age 3-23 months were conducted and overall a higher proportion of detectable blood levels was seen in the pediatric patient population as compared to the adult patient population following twice daily application of Elidel for 3 weeks. Therefore, taking safety for the infant population into consideration, Elidel will be covered for mild to moderate AD for short-term use, up to 3 months.

According to the AAD psoriasis guidelines, TCS are the cornerstone of treatment for the majority of patients with psoriasis, particularly those with limited disease. Lower potency corticosteroids should generally be used for limited periods of time on the face, intertriginous areas, areas with thin skin, and in infants. In other areas and in adults, mid- or high-potency agents are generally recommended as initial therapy. Patients with thick, chronic plaques often require treatment with the highest potency corticosteroids. The compendia indicate use of TCI in psoriasis, however per AAD guidelines, even though TCI are generally not effective for plaque psoriasis, they may be used on thinner skin areas to treat facial and intertriginous psoriasis with no evidence of resultant skin atrophy as compared with the use of topical corticosteroids in these regions.

Based on the Cochrane review on interventions for vitiligo, TCI seem to be a reasonable alternative to TCS, particularly on anatomical sites where there may be a higher risk of adverse effects with TCS. Standardized methodologies for describing and classifying vitiligo and for assessing the effect of interventions need to be developed and used by trial investigators. The establishment of a Vitiligo European Task Force (VETF) is an important step in this direction and the work of this group should hopefully lead to studies measuring repigmentation in a more standardized way. However, many studies still use their own measures, so the work of the VETF group needs to be disseminated as widely as possible. The guidelines developed by this taskforce recommend that TCI be considered in adults and children with vitiligo as an alternative to topical steroids due to better safety profile, and restricted to selected areas, in particular the head and neck region.

REFERENCES
CRITERIA FOR APPROVAL

1. Is the requested drug being prescribed for mild to moderate atopic dermatitis (eczema)?
   Yes No
   [If no, then skip to question 5.]

2. Will the requested drug be used around the eyes, on the face, genitals, or skin folds?
   Yes No
   [If yes, then no further questions.]

3. Has the patient experienced an inadequate treatment response, intolerance, or contraindication to at least one first line therapy agent (e.g., medium or higher potency topical corticosteroid)?
   Yes No
   [If yes, then no further questions.]

4. Is the patient less than 2 years of age AND unable to use a first line therapy agent (e.g., medium or higher potency topical corticosteroid)?
   Yes No
   [No further questions.]

5. Is the requested drug being prescribed for psoriasis on the face, genitals, or skin folds OR vitiligo on the head or neck?
   Yes No

Mapping Instructions (759-A)

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
<th>DENIAL REASONS – DO NOT USE FOR MEDICARE PART D</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Go to 2</td>
<td>Go to 5</td>
<td>You do not meet the requirements of your plan.</td>
</tr>
<tr>
<td>2. Approve for 36 months</td>
<td>Go to 3</td>
<td>Your plan covers this drug when you meet any of these conditions:</td>
</tr>
<tr>
<td>3. Approve for 36 months</td>
<td>Go to 4</td>
<td>- You have atopic dermatitis (eczema) around the eyes, on the face, genitals, or skin folds</td>
</tr>
<tr>
<td>4. Approve for 3 months</td>
<td>Deny</td>
<td>- You tried a first line drug for atopic dermatitis (eczema) and it did not work for you or you cannot use it (examples of first line drugs are medium or stronger steroid creams or ointments)</td>
</tr>
<tr>
<td>5. Approve for 36 months</td>
<td>Deny</td>
<td>- You are less than 2 years of age and cannot use a first line drug (examples of first line drugs are medium or stronger steroid creams or ointments)</td>
</tr>
</tbody>
</table>

Your request has been denied based on the information we have.
[Short Description: No inadequate response, intolerance or contraindication to first line agents (e.g., medium or higher potency topical corticosteroids)]

Your plan covers this drug when you have any of these conditions:
- Mild to moderate atopic dermatitis (eczema)
- Psoriasis on the face, genitals, or skin folds
- Vitiligo on the head or neck
Your request has been denied based on the information we have.
[Short Description: No approvable diagnosis]
### Guidelines for Approval (MDC-2 491-A)

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<th>Duration of Approval</th>
<th>12 Months</th>
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</tr>
<tr>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td></td>
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**Duration of Approval**

<table>
<thead>
<tr>
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</thead>
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<tr>
<td><strong>Set 1</strong></td>
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<tr>
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</tr>
<tr>
<td>4</td>
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### Mapping Instructions (MDC-2 491-A)

<table>
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<tr>
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<th>No</th>
<th>DENIAL REASONS – DO NOT USE FOR MEDICARE PART D</th>
</tr>
</thead>
<tbody>
<tr>
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<td>Go to 2</td>
<td>Go to 5</td>
</tr>
<tr>
<td>2.</td>
<td>Approve for 12 months</td>
<td>Go to 5</td>
</tr>
<tr>
<td>3.</td>
<td>Approve for 12 months</td>
<td>Go to 4</td>
</tr>
<tr>
<td>4.</td>
<td>Approve for 3 months</td>
<td>Deny</td>
</tr>
</tbody>
</table>

**You do not meet the requirements of your plan.**

Your plan covers this drug when you meet any of these conditions:
- You have atopic dermatitis (eczema) around the eyes, on the face, genitals, or skin folds
- You tried a first line drug for atopic dermatitis (eczema) and it did not work for you or you cannot use it (examples of first line drugs are medium or stronger steroid creams or ointments)
- You are less than 2 years of age and cannot use a first line drug (examples of first line drugs are medium or stronger steroid creams or ointments)

Your request has been denied based on the information we have.

[Short Description: No inadequate response, intolerance or contraindication to first line agents (e.g., medium or higher potency topical corticosteroids)]

| 5.  | Approve for 12 months | Deny |

**You do not meet the requirements of your plan.**

Your plan covers this drug when you have any of these conditions:
- Mild to moderate atopic dermatitis (eczema)
- Psoriasis on the face, genitals, or skin folds
- Vitiligo on the head or neck

Your request has been denied based on the information we have.

[Short Description: No approvable diagnosis]
SPECIALTY GUIDELINE MANAGEMENT

ELIGARD (leuprolide acetate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
   Palliative treatment of advanced prostate cancer

B. Compendial Uses
   1. Prostate cancer
   2. Metastatic androgen receptor positive salivary gland tumors
   3. Gender Dysphoria (also known as gender non-conforming or transgender persons)
      
      NOTE: Some plans may opt-out of coverage for gender dysphoria.

   All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Prostate cancer
   Authorization of 12 months may be granted for treatment of prostate cancer.

B. Gender dysphoria
   1. Authorization of 12 months may be granted for pubertal suppression in preparation for gender reassignment in an adolescent member when all of the following criteria are met:
      a. The member has a diagnosis of gender dysphoria.
      b. The member has reached Tanner stage 2 of puberty.
   2. Authorization of 12 months may be granted for gender reassignment in an adult member when all of the following criteria are met:
      a. The member has a diagnosis of gender dysphoria.
      b. The member will receive Eligard concomitantly with cross sex hormones.

C. Salivary gland tumors
   Authorization of 12 months may be granted for treatment of metastatic salivary gland tumors when the tumor is androgen receptor positive.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.
IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

ELZONRIS (tagraxofusp-erzs)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Elzonris is a CD123-directed cytotoxin for the treatment of blastic plasmacytoid dendritic cell neoplasm (BPDCN) in adults and in pediatric patients 2 years and older.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Blastic plasmacytoid dendritic cell neoplasm (BPDCN)
Authorization of 12 months may be granted for treatment of blastic plasmacytoid dendritic cell neoplasm (BPDCN) when the patient’s disease is positive for CD123 expression.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

EMFLAZA (deflazacort)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Emflaza is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients 2 years of age and older.

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Laboratory confirmation of DMD diagnosis by genetic testing.

B. Chart documentation of weight gain/obesity or persistent psychiatric/behavioral issues with previous prednisone treatment.

III. CRITERIA FOR INITIAL APPROVAL

Duchenne Muscular Dystrophy

Authorization of 6 months may be granted for treatment of DMD when all of the following criteria are met:

A. The diagnosis of DMD was confirmed by genetic testing demonstrating a mutation in the DMD gene.

B. The member is 2 years of age or older.

C. The member has tried prednisone and experienced unmanageable and clinically significant weight gain/obesity or psychiatric/behavioral issues (e.g., abnormal behavior, aggression, irritability).
   1. For weight gain/obesity: body mass index is in the overweight or obese category while receiving treatment with prednisone (refer to Appendix for weight status categories for children and adults).
   2. For psychiatric/behavioral issues: psychiatric/behavioral issues persisted beyond the first 6 weeks of treatment with prednisone.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members requesting continuation of therapy when all of the following criteria are met:

A. The member meets initial authorization criteria.

B. The member is receiving a clinical benefit from Emflaza therapy, such as improvement or stabilization of muscle strength or pulmonary function.
V. APPENDIX

Body Mass Index Percentile and Weight Status Category for Children 2 Through 19 Years of Age

<table>
<thead>
<tr>
<th>Body Mass Index Percentile Range</th>
<th>Weight Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than the 5th percentile</td>
<td>Underweight</td>
</tr>
<tr>
<td>5th percentile to less than the 85th percentile</td>
<td>Normal or Healthy Weight</td>
</tr>
<tr>
<td>85th to less than the 95th percentile</td>
<td>Overweight</td>
</tr>
<tr>
<td>Equal to or greater than the 95th percentile</td>
<td>Obese</td>
</tr>
</tbody>
</table>

Body Mass Index and Weight Status Category for Adults (20 Years of Age and Older)

<table>
<thead>
<tr>
<th>Body Mass Index</th>
<th>Weight Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Below 18.5</td>
<td>Underweight</td>
</tr>
<tr>
<td>18.5 – 24.9</td>
<td>Normal or Healthy Weight</td>
</tr>
<tr>
<td>25.0 – 29.9</td>
<td>Overweight</td>
</tr>
<tr>
<td>30.0 and Above</td>
<td>Obese</td>
</tr>
</tbody>
</table>

VI. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

EMPLICITI (elotuzumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Empliciti is indicated in combination with lenalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received one to three prior therapies.
   2. Empliciti is indicated in combination with pomalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor.

B. Compendial Uses
   Therapy for previously treated multiple myeloma for relapsed or progressive disease in combination with bortezomib and dexamethasone

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Multiple Myeloma
Authorization of 12 months may be granted for the treatment of multiple myeloma for members who have received at least one prior therapy.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

ENBREL (etanercept)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Moderately to severely active rheumatoid arthritis (RA)
   2. Moderately to severely active polyarticular juvenile idiopathic arthritis (pJIA)
   3. Active psoriatic arthritis (PsA)
   4. Active ankylosing spondylitis (AS)
   5. Moderate to severe chronic plaque psoriasis (PsO)

B. Compendial Uses
   1. Axial spondyloarthritis
   2. Reactive arthritis
   3. Hidradenitis suppurativa, severe, refractory

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active rheumatoid arthritis (RA)
   1. Authorization of 24 months may be granted for members who have previously received Enbrel or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) indicated for moderately to severely active rheumatoid arthritis.
   2. Authorization of 24 months may be granted for treatment of moderately to severely active RA when any of the following criteria is met:
      a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
      b. Member has an intolerance or contraindication to methotrexate (see Appendix A).

B. Moderately to severely active polyarticular juvenile idiopathic arthritis (pJIA)
   1. Authorization of 24 months may be granted for members who have previously received Enbrel or any other biologic DMARD indicated for moderately to severely active polyarticular juvenile idiopathic arthritis.
   2. Authorization of 24 months may be granted for treatment of active pJIA when any of the following criteria is met:
      a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate.
      b. Member has intolerance or contraindication to methotrexate (see Appendix A).
C. Active psoriatic arthritis (PsA)
Authorization of 24 months may be granted for treatment of active psoriatic arthritis (PsA).

D. Active ankylosing spondylitis (AS) and axial spondyloarthritis
1. Authorization of 24 months may be granted for members who have previously received Enbrel or any other biologic DMARD indicated for active ankylosing spondylitis.

2. Authorizations of 24 months may be granted for treatment of active ankylosing spondylitis and axial spondyloarthritis when any of the following criteria is met:
   a. Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs).
   b. Member has an intolerance or contraindication to two or more NSAIDs.

E. Moderate to severe chronic plaque psoriasis
1. Authorization of 24 months may be granted for members who have previously received Enbrel, Otezla, or any other biologic DMARD indicated for the treatment of moderate to severe chronic plaque psoriasis.

2. Authorization of 24 months may be granted for treatment of moderate to severe chronic plaque psoriasis when all of the following criteria are met:
   a. At least 5% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
   b. Member meets any of the following criteria:
      i. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
      ii. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine or acitretin (see Appendix B).
      iii. Member has severe psoriasis that warrants a biologic DMARD as first-line therapy.

F. Reactive arthritis
Authorization of 24 months may be granted for treatment of reactive arthritis.

G. Hidradenitis suppurativa
Authorization of 24 months may be granted for treatment of severe, refractory hidradenitis suppurativa.

III. CONTINUATION OF THERAPY
Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Enbrel as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER
For all indications: Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB).

Note: Members who have received Enbrel or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) are exempt from all requirements related to TB screening in this Policy.
V. APPENDICES

Appendix A: Examples of Contraindications to Methotrexate
1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy
10. Renal impairment
11. Significant drug interaction

Appendix B: Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin.
1. Alcoholism, alcoholic liver disease, or other chronic liver disease
2. Breastfeeding
3. Drug interaction
4. Cannot be used due to risk of treatment-related toxicity
5. Pregnancy or planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VI. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

ENDARI (L-glutamine oral powder)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Endari is indicated to reduce the acute complications of sickle cell disease in adult and pediatric patients 5 years of age and older.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Sickle cell disease
Authorization of 12 months may be granted for use in reducing the acute complications of sickle cell disease in members 5 years of age or older.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

ENTYVIO (vedolizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Moderately to severely active ulcerative colitis (UC)
2. Moderately to severely active Crohn’s disease (CD)

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active ulcerative colitis (UC)

1. Authorization of 4 months may be granted for members who are 18 years of age or older who have previously received Entyvio or any other biologic or targeted synthetic drug (e.g., Xeljanz) indicated for moderately to severely active ulcerative colitis.

2. Authorization of 4 months may be granted for treatment of moderately to severely active UC in members who are 18 years of age or older who had an inadequate response, intolerance or contraindication to EITHER of the following:
   a. At least ONE conventional therapy option (See Appendix A)
   b. At least ONE TNF-alpha inhibitor indicated for UC:
      i. Humira (adalimumab)
      ii. Remicade (infliximab)
      iii. Simponi (golimumab)

B. Moderately to severely active Crohn’s disease (CD)

1. Authorization of 4 months may be granted for members who are 18 years of age or older who have previously received Entyvio or any other biologic indicated for the treatment of Crohn’s disease.

2. Authorization of 4 months may be granted for treatment of moderately to severely active CD in members who are 18 years of age or older who had an inadequate response, intolerance or contraindication to EITHER of the following:
   a. At least ONE conventional therapy option (See Appendix B)
   b. At least ONE TNF-alpha inhibitor indicated for CD:
      i. Cimzia (certolizumab)
      ii. Humira (adalimumab)
      iii. Remicade (infliximab)
III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 4 months of therapy with Entyvio as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. APPENDICES

Appendix A: Examples of Conventional Therapy Options for UC

1. Mild to moderate disease – induction of remission:
   a. Oral mesalamine (e.g., Asacol, Asacol HD, Lialda, Pentasa), balsalazide, olsalazine
   b. Rectal mesalamine (e.g., Canasa, Rowasa)
   c. Rectal hydrocortisone (e.g., Colocort, Cortifoam)
   d. Alternatives: prednisone, azathioprine, mercaptopurine, sulfasalazine

2. Mild to moderate disease – maintenance of remission:
   a. Oral mesalamine, balsalazide, olsalazine, rectal mesalamine
   b. Alternatives: azathioprine, mercaptopurine, sulfasalazine

3. Severe disease – induction of remission:
   a. Prednisone, hydrocortisone IV, methylprednisolone IV
   b. Alternatives: cyclosporine IV, tacrolimus, sulfasalazine

4. Severe disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: sulfasalazine

5. Pouchitis: Metronidazole, ciprofloxacin
   a. Alternative: rectal mesalamine

Appendix B: Examples of Conventional Therapy Options for CD

1. Mild to moderate disease – induction of remission:
   a. Oral budesonide
   b. Alternatives: metronidazole, ciprofloxacin, rifaximin

2. Mild to moderate disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternatives: oral budesonide, methotrexate intramuscular (IM) or subcutaneous (SC), sulfasalazine

3. Moderate to severe disease – induction of remission:
   a. Prednisone, methylprednisolone intravenously (IV)
   b. Alternatives: methotrexate IM or SC

4. Moderate to severe disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: methotrexate IM or SC

5. Perianal and fistulizing disease – induction of remission
   a. Metronidazole ± ciprofloxacin, tacrolimus

6. Perianal and fistulizing disease – maintenance of remission
   a. Azathioprine, mercaptopurine
   b. Alternative: methotrexate IM or SC

V. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

EPCLUSA (sofosbuvir and velpatasvir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Epclusa is indicated for the treatment of adult patients with chronic hepatitis C virus (HCV) genotype 1, 2, 3, 4, 5 or 6 infection:
A. without cirrhosis or with compensated cirrhosis
B. with decompensated cirrhosis for use in combination with ribavirin

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR APPROVAL

A. Chronic hepatitis C virus infection, without ribavirin
   1. Genotype 1 infection
      a. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naive or who failed prior treatment with peginterferon alfa (PEG-IFN) and ribavirin (RBV) with or without an HCV protease inhibitor (boceprevir, simeprevir or telaprevir).
      b. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have genotype 1b infection and who failed prior treatment with non-NS5A inhibitor, sofosbuvir-containing regimen.
   2. Genotype 2 infection
      a. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naive or who failed prior treatment with PEG-IFN and RBV.
      b. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with sofosbuvir (Sovaldi) and ribavirin.
   3. Genotype 3 infection
      Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naive or who failed prior treatment with PEG-IFN and RBV.
   4. Genotype 4, 5 or 6 infection
      Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naive or who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor (boceprevir, simeprevir or telaprevir).
5. ** Decompensated cirrhosis (Child Turcotte Pugh [CTP] class B or C)**
   Authorization of up to 24 weeks total may be granted for members with genotype 1, 2, 3, 4, 5 or 6 infection who have decompensated cirrhosis and documented anemia (baseline hemoglobin [Hgb] below 10 g/dL) or RBV ineligibility (see Section IV).

B. **Chronic hepatitis C virus infection, in combination with ribavirin**
   1. **Genotype 3 infection**
      a. Authorization of up to 12 weeks total may be granted for members with the Y93H substitution associated with velpatasvir resistance who are either of the following:
         i. Treatment-naïve with compensated cirrhosis
         ii. Failed prior treatment with PEG-IFN and RBV without cirrhosis
      b. Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV.

   2. ** Decompensated cirrhosis (CTP class B or C)**
      a. Authorization of up to 12 weeks total may be granted for members with genotype 1, 2, 3, 4, 5 or 6 infection and decompensated cirrhosis.
      b. Authorization of up to 24 weeks total may be granted for members with genotype 1, 2, 3, 4, 5 or 6 infection and decompensated cirrhosis who failed prior treatment with a sofosbuvir- or NS5A inhibitor-based regimen.

   3. ** Recurrent HCV infection post liver transplantation**
      Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis or decompensated cirrhosis and recurrent HCV genotype 2 or 3 infection post liver transplantation.

C. **HCV and HIV coinfection**
   Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A or B above are met.

III. **CONTINUATION OF THERAPY**
   All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. **APPENDIX: RIBAVIRIN INELIGIBILITY**
   RBV ineligibility is defined as one or more of the below:
   - Intolerance to RBV
   - Pregnant female or male whose female partner is pregnant
   - Hemoglobinopathy
   - Coadministration with didanosine
   - History of significant or unstable cardiac disease

V. **REFERENCES**
SPECIALTY GUIDELINE MANAGEMENT

EPIDIOLEX (cannabidiol)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Epidiolex is indicated for the treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients 2 years of age and older.

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review:

• For new starts only:
  o Prior and current antiepileptic therapy
  o Medical record documentation (i.e., chart notes or laboratory report) indicating the clinical assessments outlined in section IV have been performed.

• For new starts and continuation requests: Medical record documentation (i.e., chart notes, imaging report, or laboratory report) of electroencephalography (EEG), magnetic resonance imaging (MRI), or SCN1A gene mutation

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a neurologist.

IV. CRITERIA FOR INITIAL APPROVAL

Seizures associated with Lennox-Gastaut syndrome or Dravet syndrome

Authorization of 6 months may be granted for treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome when all of the following criteria are met:

A. Member has a documented inadequate response to prior therapy with at least one anti-epileptic drug.
   Examples of antiepileptic drugs:
   • For Lennox-Gastaut syndrome: clobazam, felbamate, lamotrigine, levetiracetam, topiramate, rufinamide, valproate
   • For Dravet syndrome: clobazam, levetiracetam, stiripentol, topiramate, valproate

B. Epidiolex will be used in combination with one or more anti-epileptic drugs.

C. Member has received documented clinical assessments that include all of the following:
   1. EEG, MRI, or SCN1A gene mutation confirmed by genetic testing
   2. Age at seizure onset, seizure types, and frequency of episodes
3. Review of risk factors, other causes of seizures (e.g., other medical conditions and medications), family history, and developmental history

V. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who meet both of the following:

A. Documentation of EEG, MRI, or SCN1A gene mutation confirmed by genetic testing has been submitted
B. Member has achieved and maintained positive clinical response with Epidiolex therapy as evidenced by reduction in frequency or duration of seizures

VI. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

EPOGEN, PROCRIT, RETACRIT (epoetin alfa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Epoetin alfa is indicated for the treatment of anemia due to chronic kidney disease (CKD), including patients on dialysis and not on dialysis to decrease the need for red blood cell (RBC) transfusion.
2. Epoetin alfa is indicated for the treatment of anemia due to zidovudine administered at ≤ 4200 mg/week in HIV-infected patients with endogenous serum erythropoietin levels of ≤ 500 mUnits/mL.
3. Epoetin alfa is indicated for the treatment of anemia in patients with non-myeloid malignancies where anemia is due to the effect of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy.
4. Epoetin alfa is indicated to reduce the need for allogeneic RBC transfusions among patients with perioperative hemoglobin > 10 to ≤ 13 g/dL who are at high risk for perioperative blood loss from elective, noncardiac, nonvascular surgery. Epoetin alfa is not indicated for patients who are willing to donate autologous blood preoperatively.

B. Compendial Uses
1. Symptomatic anemia in patients with myelodysplastic syndromes (MDS)
2. Anemia in congestive heart failure
3. Anemia in rheumatoid arthritis
4. Anemia due to hepatitis C treatment with ribavirin in combination with either interferon alfa or peginterferon alfa
5. Anemia in patients whose religious beliefs forbid blood transfusions
6. Symptomatic anemia in patients with primary myelofibrosis, post-polycythemia vera myelofibrosis, and post-essential thrombocythemia myelofibrosis
7. Cancer patients who are undergoing palliative treatment

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Note: Requirements regarding pretreatment hemoglobin level exclude values due to a recent transfusion. All members must be assessed for iron deficiency anemia and have adequate iron stores or are receiving iron therapy before starting Epogen/Procrit/Retacrit. Members may not use Epogen/Procrit/Retacrit concomitantly with other erythropoiesis stimulating agents.

A. Anemia Due to CKD
Authorization of 12 weeks may be granted for members with pretreatment hemoglobin < 10 g/dL.

B. Anemia Due to Myelosuppressive Chemotherapy
Authorization of 12 weeks may be granted for members with nonmyeloid malignancy with pretreatment hemoglobin < 10 g/dL.

C. Anemia in MDS
Authorization of 12 weeks may be granted for members with pretreatment hemoglobin < 10 g/dL whose pretreatment serum EPO level is < 500 mU/mL.

D. Reduction of Allogeneic Red Blood Cell Transfusion in Patients Undergoing Elective, Noncardiac, Nonvascular Surgery
Authorization of 30 days may be granted for members scheduled to have an elective, noncardiac, nonvascular surgery when the pretreatment hemoglobin is ≤ 13 g/dL.

E. Anemia in Congestive Heart Failure (CHF)
Authorization of 12 weeks may be granted for members with pretreatment hemoglobin < 9 g/dL.

F. Anemia in Rheumatoid Arthritis (RA)
Authorization of 12 weeks may be granted for members with pretreatment hemoglobin < 10 g/dL.

G. Anemia Due to Hepatitis C Treatment
Authorization of 12 weeks may be granted for members with pretreatment hemoglobin < 10 g/dL who are receiving ribavirin in combination with either interferon alfa or peginterferon alfa.

H. Anemia Due to Zidovudine in HIV-infected Patients
Authorization of 12 weeks may be granted for members currently receiving zidovudine with pretreatment hemoglobin < 10 g/dL whose pretreatment serum EPO level is < 500 mU/mL.

I. Anemia in Members Whose Religious Beliefs Forbid Blood Transfusions
Authorization of 12 weeks may be granted for members with pretreatment hemoglobin < 10 g/dL.

J. Anemia in Primary Myelofibrosis (MF), Post-polycythemia Vera MF, and Post-Essential Thrombocythemia MF
Authorization of 12 weeks may be granted for members who meet ALL of the following criteria:
1. Pretreatment hemoglobin < 10 g/dL
2. Pretreatment serum erythropoietin level < 500 mU/mL

K. Anemia Due to Cancer
Authorization of 12 weeks may be granted for members who have cancer and are undergoing palliative treatment

III. CONTINUATION OF THERAPY

Note: Requirements regarding current hemoglobin level exclude values due to a recent transfusion. Members may not use Epogen/Procrit/Retacrit concomitantly with other erythropoiesis stimulating agents.

For all indications below: all members (including new members) requesting authorization for continuation of therapy after at least 12 weeks of ESA treatment must show a response with a rise in hemoglobin of ≥ 1 g/dL. Members who completed less than 12 weeks of ESA treatment and have not yet responded with a rise in
hemoglobin of $\geq 1$ g/dL may be granted authorization of up to 12 weeks to allow for sufficient time to demonstrate a response.

A. **Anemia Due to CKD**
   Authorization of 12 weeks may be granted for continuation of therapy when the current hemoglobin is $< 12$ g/dL.

B. **Anemia Due to Myelosuppressive Chemotherapy**
   Authorization of 12 weeks may be granted for the continuation of therapy in members with nonmyeloid malignancy with current hemoglobin is $< 12$ g/dL.

C. **Anemia in MDS**
   Authorization of 12 weeks may be granted for continuation of treatment when the current hemoglobin is $< 12$ g/dL.

D. **Anemia in CHF, RA**
   Authorization of 12 weeks may be granted for continuation of treatment when the current hemoglobin is $< 12$ g/dL.

E. **Anemia Due to Hepatitis C Treatment**
   Authorization of 12 weeks may be granted for continuation of treatment when the member meets ALL of the following criteria:
   1. The member is receiving ribavirin in combination with either interferon alfa or peginterferon alfa
   2. The current hemoglobin is $\leq 12$ g/dL.

F. **Anemia Due to Zidovudine in HIV-infected Patients**
   Authorization of 12 weeks may be granted for continuation of therapy in members receiving zidovudine when the current hemoglobin is $\leq 12$ g/dL.

G. **Anemia in Members Whose Religious Beliefs Forbid Blood Transfusions**
   Authorization of 12 weeks may be granted for continuation of treatment when the current hemoglobin is $\leq 12$ g/dL.

H. **Anemia in Primary Myelofibrosis, Post-polycythemia Vera Myelofibrosis, and Post-Essential Thrombocythemia Myelofibrosis**
   Authorization of 12 weeks may be granted for continuation of treatment when the current hemoglobin is $\leq 12$ g/dL.

I. **Anemia Due to Cancer**
   Authorization of 12 weeks may be granted for members who have cancer and are undergoing palliative treatment

IV. REFERENCES
3. Retacrit [package insert]. Lake Forest, IL: Hospira Inc.; May 2018


SPECIALTY GUIDELINE MANAGEMENT

Flolan (epoprostenol for injection)
Veletri (epoprostenol for injection)
eoprostenol for injection (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Epoprostenol/Flolan/Veletri is indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group I) to improve exercise capacity. Studies establishing effectiveness included predominantly patients with NYHA Functional Class III-IV symptoms and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Indefinite authorization may be granted for treatment of PAH when ALL of the following criteria are met:
A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
B. PAH was confirmed by either criterion (1) or criterion (2) below:
   1. Pretreatment right heart catheterization with all of the following results:
      i. mPAP ≥ 25 mmHg
      ii. PCWP ≤ 15 mmHg
      iii. PVR > 3 Wood units

   2. For infants less than one year of age with any of the following conditions, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed:
      i. Post cardiac surgery
      ii. Chronic heart disease
      iii. Chronic lung disease associated with prematurity
      iv. Congenital diaphragmatic hernia

III. CONTINUATION OF THERAPY

Indefinite authorization may be granted for members with an indication listed in Section II who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. APPENDIX
WHO Classification of Pulmonary Hypertension

1 PAH
1.1 Idiopathic (PAH)
1.2 Heritable PAH
1.3 Drug- and toxin-induced PAH
1.4. PAH associated with:
   1.4.1 Connective tissue diseases
   1.4.2 HIV infection
   1.4.3 Portal hypertension
   1.4.4 Congenital heart diseases
   1.4.5 Schistosomiasis
1.5 PAH long-term responders to calcium channel blockers
1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease
2.1 PH due to heart failure with preserved LVEF
2.2 PH due to heart failure with reduced LVEF
2.3 Valvular heart disease
2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia
3.1 Obstructive lung disease
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction
4.1 Chronic thromboembolic PH
4.2 Other pulmonary artery obstructions
   4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
   4.2.2 Other malignant tumors
      Renal carcinoma
      Uterine carcinoma
      Germ cell tumours of the testis
      Other tumours
   4.2.3 Non-malignant tumours
      Uterine leiomyoma
   4.2.4 Arteritis without connective tissue disease
   4.2.5 Congenital pulmonary artery stenosis
   4.2.6 Parasites
      Hydatidosis

5 PH with unclear and/or multifactorial mechanisms
5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
5.4 Complex congenital heart disease

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

ERBITUX® (cetuximab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Erbitux is an epidermal growth factor receptor (EGFR) antagonist indicated for treatment of:

1. Head and Neck Cancer
   a. In combination with radiation therapy (RT) for the treatment of locally or regionally advanced squamous cell carcinoma of the head and neck
   b. In combination with platinum-based therapy with 5-fluorouracil (5FU) for the treatment of patients with recurrent locoregional disease or metastatic squamous cell carcinoma of the head and neck
   c. For treatment of recurrent or metastatic squamous cell carcinoma of the head and neck for whom prior platinum-based therapy has failed

2. Colorectal Cancer

   KRAS mutation-negative (wild-type), EGFR-expressing, metastatic colorectal cancer (mCRC) as determined by FDA-approved tests for this use:
   a. In combination with FOLFIRI for first-line treatment
   b. In combination with irinotecan in patients who are refractory to irinotecan-based chemotherapy
   c. As a single agent in patients who have failed oxaliplatin- and irinotecan-based chemotherapy or who are intolerant to irinotecan

Limitations of Use:

Erbitux is not indicated for treatment of Ras-mutant colorectal cancer or when the results of the Ras mutation tests are unknown.

B. Compendial Uses

1. Colorectal cancer
2. Penile cancer
3. Squamous cell skin cancer
4. Non-small cell lung cancer

II. CRITERIA FOR INITIAL APPROVAL

A. Colorectal Cancer

Authorization of 12 months may be granted for treatment of colorectal cancer when the following criteria are met:

1. Tumor is negative (wild-type) for RAS (KRAS and NRAS) mutations.
2. Member has not previously experienced clinical failure on panitumumab.
B. **Head and Neck Cancer**  
Authorization of 12 months may be granted for treatment of head and neck cancer.

C. **Penile Cancer**  
Authorization of 12 months may be granted for treatment of metastatic penile cancer.

D. **Squamous Cell Skin Cancer**  
Authorization of 12 months may be granted for treatment of recurrent or metastatic squamous cell skin cancer.

E. **Non-Small Cell Lung Cancer (NSCLC)**  
Authorization of 12 months may be granted for treatment of metastatic NSCLC in members with a known sensitizing EGFR mutation (e.g., EGFR exon 19 deletion or exon 21 (L858R, L861) mutation) when Erbitux is used following disease progression on EGFR tyrosine kinase inhibitor therapy (e.g., afatinib, erlotinib, gefitinib).

III. **CONTINUATION OF THERAPY**

All members (including new members) requesting authorization for continuation therapy must meet all initial authorization criteria.

IV. **REFERENCES**

SPECIALTY GUIDELINE MANAGEMENT

ERIVEDGE (vismodegib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Erivedge is indicated for the treatment of adults with metastatic basal cell carcinoma, or with locally advanced basal cell carcinoma that has recurred following surgery or who are not candidates for surgery, and who are not candidates for radiation.

B. Compendial Uses
Nodal or distant metastatic basal cell carcinoma

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Basal Cell Carcinoma (BCC)
Authorization of 12 months may be granted for the treatment of locally advanced or metastatic basal cell carcinoma.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in Section II when there is no evidence of unacceptable toxicity or disease progression on the current regimen.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

ERLEADA (apalutamide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Erleada is indicated for the treatment of patients with non-metastatic castration-resistant prostate cancer.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Non-metastatic castration-resistant prostate cancer
Authorization of 24 months may be granted for treatment of non-metastatic castration-resistant prostate cancer when Erleada will be administered with a gonadotropin-releasing hormone (GnRH) analog or after bilateral orchiectomy.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

ERWINAZE (asparaginase Erwinia chrysanthemi)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
Erwinaze is indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of patients with acute lymphoblastic leukemia (ALL) who have developed hypersensitivity to E. coli-derived asparaginase.

B. Compendial Uses
Lymphoblastic lymphoma (managed in the same manner as ALL)

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for the treatment of acute lymphoblastic leukemia or lymphoblastic lymphoma when all of the following criteria are met:

A. Erwinaze will be used in conjunction with multi-agent chemotherapy.
B. The member has previously received and developed hypersensitivity to an E. coli-derived asparaginase (eg, Oncaspar).

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

ESBRIET (pirfenidone)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Esbriet is indicated for the treatment of idiopathic pulmonary fibrosis.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Idiopathic Pulmonary Fibrosis (IPF)
Authorization of 24 months may be granted for treatment of idiopathic pulmonary fibrosis when the member has undergone a diagnostic work-up which includes the following:

1. Other known causes of interstitial lung disease (e.g., domestic and occupational environmental exposures, connective tissue disease, drug toxicity) have been excluded AND
2. The member has completed a high-resolution computed tomography (HRCT) study of the chest or a lung biopsy which reveals a result consistent with the usual interstitial pneumonia (UIP) pattern, OR has completed an HRCT study of the chest which reveals a result other than the UIP pattern (e.g., probable UIP, indeterminate for UIP) and the diagnosis is supported by a lung biopsy. If a lung biopsy has not been previously conducted, the diagnosis is supported by a multidisciplinary discussion between a radiologist and pulmonologist who are experienced in IPF.

III. CONTINUATION OF THERAPY

Idiopathic Pulmonary Fibrosis (IPF)
All members (including new members) requesting authorization for continuation of therapy may be granted an authorization of 24 months when the member is currently receiving treatment with Esbriet, excluding when Esbriet is obtained as samples or via manufacturer’s patient assistance programs.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

EVENITY (romosozumab-aqqg)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Evenity is indicated for the treatment of osteoporosis in postmenopausal women at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy.

Limitations of Use: Limit duration of use to 12 monthly doses. If osteoporosis therapy remains warranted, continued therapy with an anti-resorptive agent should be considered.

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Supporting chart notes or medical record indicating a history of fragility fractures, T-score, and FRAX fracture probability as applicable to section III.

III. CRITERIA FOR INITIAL APPROVAL

Postmenopausal osteoporosis treatment
Authorization of a total of 12 months may be granted to postmenopausal members with osteoporosis when ANY of the following criteria are met:

A. Member has a history of fragility fractures

B. Member has a pre-treatment T-score less than or equal to -2.5 OR member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B) and meets ANY of the following criteria:
   1. Member has indicators of higher fracture risk (e.g., advanced age, frailty, glucocorticoid use, very low T-scores [less than or equal to -3.5], or increased fall risk)
   2. Member has failed prior treatment with or is intolerant to previous injectable osteoporosis therapy (e.g., zoledronic acid [Reclast], teriparatide [Forteo], denosumab [Prolia])
   3. Member has had an oral bisphosphonate trial of at least 1-year duration or there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)
IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria AND have received less than 12 monthly doses of Evenity.

V. APPENDIX

Appendix A. Clinical reasons to avoid oral bisphosphonate therapy
- Esophageal abnormality that delays emptying such as stricture of achalasia
- Active upper gastrointestinal problem (e.g., dysphagia, gastritis, duodenitis, erosive esophagitis, ulcers)
- Inability to stand or sit upright for at least 30 to 60 minutes
- Inability to take at least 30 to 60 minutes before first food, drink, or medication of the day
- Renal insufficiency (creatinine clearance <35 mL/min)
- History of intolerance to an oral bisphosphonate

Appendix B. WHO Fracture Risk Assessment Tool
- High FRAX fracture probability: 10 year major osteoporotic fracture risk ≥ 20% or hip fracture risk ≥ 3%.
- 10-year probability; calculation tool available at: https://www.sheffield.ac.uk/FRAX/
- The estimated risk score generated with FRAX should be multiplied by 1.15 for major osteoporotic fracture and 1.2 for hip fracture if glucocorticoid treatment is greater than 7.5 mg per day.

VI. REFERENCES

<table>
<thead>
<tr>
<th>BRAND NAME* (generic)</th>
<th>EVZIO (naloxone hydrochloride injection)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NARCAN NASAL SPRAY (naloxone hydrochloride nasal spray)</td>
</tr>
</tbody>
</table>

**Status:** CVS Caremark Criteria  
**Type:** Quantity Limit  
**Ref # 1137-H**

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

**FDA-APPROVED INDICATIONS**

**Evzio**
Evzio is an opioid antagonist indicated for the emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression. Evzio is intended for immediate administration as emergency therapy in settings where opioids may be present. Evzio is not a substitute for emergency medical care.

**Narcan Nasal Spray**
Narcan nasal spray (naloxone nasal spray) is indicated for the emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression. Narcan nasal spray (naloxone nasal spray) is intended for immediate administration as emergency therapy in settings where opioids may be present. Narcan nasal spray (naloxone nasal spray) is not a substitute for emergency medical care.

**RATIONALE**
Evzio and Narcan nasal spray (naloxone nasal spray) are indicated for the emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression. Evzio and Narcan nasal spray (naloxone nasal spray) are intended for immediate administration as emergency therapy in settings where opioids may be present. Evzio and Narcan nasal spray (naloxone nasal spray) are not a substitute for emergency medical care.1-4

Each Evzio auto-injector contains a single dose of naloxone. Evzio is supplied in a carton containing two auto-injectors. Narcan nasal spray (naloxone nasal spray) is supplied in a carton containing two packages each with a single dose intranasal spray. 1-4

Evzio automatically inserts the needle intramuscularly or subcutaneously and delivers 2 mg naloxone hydrochloride. Narcan nasal spray (naloxone nasal spray) delivers 4 mg of naloxone hydrochloride intranasally. If the desired response is not obtained after 2 or 3 minutes, another Evzio or Narcan nasal spray (naloxone nasal spray) dose may be administered. If there is still no response and additional doses are available, additional Evzio or Narcan nasal spray (naloxone nasal spray) doses may be administered every 2 to 3 minutes until emergency medical assistance arrives. If the patient responds and relapses back into respiratory depression before emergency assistance arrives, an additional dose may be administered. The requirement for repeat doses of Evzio or Narcan nasal spray (naloxone nasal spray) depends upon the amount, type, and route of administration of the opioid being antagonized. The duration of action of most opioids exceeds that of naloxone hydrochloride, and the suspected opioid overdose may occur outside of supervised medical settings.1,2

The Substance Abuse and Mental Health Services Administration (SAMHSA) Opioid Overdose Prevention Toolkit states that most patients respond to naloxone generally within 2 to 3 minutes. Patients who have taken longer-acting opioids
may require further doses or an infusion. Naloxone will continue to work for 20 to 90 minutes, but after that time, overdose symptoms may return. It is essential to get the person to an emergency department or other source of medical care as quickly as possible.5,6

According to World Health Organization (WHO), a reduction in tolerance, seen when opioid use is restarted after a period of abstinence, markedly increases the risk of an opioid overdose.6 Most patients resume opioid use within six months of opioid withdrawal and are at increased risk of overdose during the first weeks of treatment.6 The SAMHSA Medication-Assisted Treatment for Opioid Addiction Protocol supports opioid addiction as a chronic medical disorder where genetic, personal-choice, and environmental factors play a part in the etiology and course including relapse and adherence to treatment. The risk of relapse during and after tapering is significant and many patients who complete tapering from opioid medication continue to need support, especially during the first 3 to 12 months.7

In the event that the patient may need a repeat dose and/or may relapse within 6 months, an initial quantity of 2 cartons (4 auto-injectors or 4 nasal sprays) of Evzio or Narcan nasal spray (naloxone nasal spray) per 180 days will be covered without prior authorization. If the patient is requesting more than the initial quantity limit, then the claim will reject with a message indicating that a prior authorization is required.

REFERENCES


LIMIT CRITERIA

<table>
<thead>
<tr>
<th>Drug</th>
<th>1 Month Limit* and 3 Month Limit*</th>
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<tbody>
<tr>
<td>Evzio (naloxone HCl injection)</td>
<td>2 cartons (4 auto-injectors) per 180 days</td>
</tr>
<tr>
<td>Narcan Nasal Spray (naloxone HCl nasal spray)</td>
<td>2 cartons (4 nasal sprays) per 180 days</td>
</tr>
</tbody>
</table>

* The 1 month, 3 month, retail, and mail limits will be the same.
PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

EVZIO
(naloxone hydrochloride injection)

NARCAN NASAL SPRAY
(naloxone hydrochloride nasal spray)

Status: CVS Caremark Criteria
Type: Post Limit Prior Authorization Ref # 1138-J

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Evzio
Evzio is an opioid antagonist indicated for the emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression.
Evzio is intended for immediate administration as emergency therapy in settings where opioids may be present.
Evzio is not a substitute for emergency medical care.

Narcan nasal spray
Narcan nasal spray (naloxone nasal spray) is indicated for the emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression.
Narcan nasal spray (naloxone nasal spray) is intended for immediate administration as emergency therapy in settings where opioids may be present.
Narcan nasal spray (naloxone nasal spray) is not a substitute for emergency medical care.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

• The requested drug is being prescribed in the event that emergency treatment of opioid overdose may be needed AND

• The patient requires more than 2 cartons (4 auto-injectors) of Evzio or 2 cartons (4 nasal sprays) of Narcan nasal spray (naloxone nasal spray) in a 6 month period due to any of the following: A) The type of opioid that the patient is taking (e.g., buprenorphine, pentazocine, long-acting/extended-release opioids), B) The patient is living in an area that has a longer wait time for emergency medical assistance, C) The patient had an overdose episode that required the use of naloxone or the requested drug. [Note: An initial quantity of 2 cartons per 6 months of Evzio or Narcan nasal spray (naloxone nasal spray) will be covered without prior authorization.]

Quantity Limits apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Evzio and Narcan nasal spray (naloxone nasal spray) are indicated for the emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression. Evzio and Narcan nasal spray (naloxone nasal spray) are intended for immediate administration as emergency therapy in settings where opioids may be present. Evzio and Narcan nasal spray (naloxone nasal spray) are not a substitute for emergency medical care.1-4
Evzio automatically inserts the needle intramuscularly or subcutaneously and delivers 2 mg naloxone hydrochloride. Narcan nasal spray (naloxone nasal spray) delivers 4 mg of naloxone hydrochloride intranasally. If the desired response is not obtained after 2 or 3 minutes, another Evzio or Narcan nasal spray (naloxone nasal spray) dose may be administered. If there is still no response and additional doses are available, additional Evzio or Narcan nasal spray (naloxone nasal spray) doses may be administered every 2 to 3 minutes until emergency medical assistance arrives. If the patient responds and relapses back into respiratory depression before emergency assistance arrives, an additional dose may be administered. Each Evzio auto-injector contains a single dose of naloxone. Evzio is supplied in a carton containing two auto-injectors. Narcan nasal spray (naloxone nasal spray) is supplied in a carton containing two packages each with a single dose intranasal spray.¹ ²

The requirement for repeat doses of Evzio or Narcan nasal spray (naloxone nasal spray) depends upon the amount, type, and route of administration of the opioid being antagonized. Reversal of respiratory depression by partial agonists or mixed agonist/antagonists, such as buprenorphine and pentazocine, may be incomplete or require higher doses of naloxone. The duration of action of most opioids exceeds that of naloxone hydrochloride, and the suspected opioid overdose may occur outside of supervised medical settings.¹ ² The Substance Abuse and Mental Health Services Administration (SAMHSA) Opioid Overdose Prevention Toolkit states that most patients respond to naloxone generally within 2 to 3 minutes. Patients who have taken longer-acting opioids may require further doses or an infusion. Naloxone will continue to work for 20 to 90 minutes, but after that time, overdose symptoms may return. It is essential to get the person to an emergency department or other source of medical care as quickly as possible.⁵ ⁶ If the patient is living in an area of extended emergency response time or taking opioids that may require further dosing, then the post limit quantity for approval will allow for 4 cartons (8 auto-injectors or 8 nasal sprays) of Evzio or Narcan nasal spray (naloxone nasal spray).

According to World Health Organization (WHO), a reduction in tolerance, seen when opioid use is restarted after a period of abstinence, markedly increases the risk of an opioid overdose.⁶ Most patients resume opioid use within six months of opioid withdrawal and are at increased risk of overdose during the first weeks of treatment.⁶ The SAMHSA Medication-Assisted Treatment for Opioid Addiction Protocol supports opioid addiction as a chronic medical disorder where genetic, personal-choice, and environmental factors play a part in the etiology and course including relapse and adherence to treatment. The risk of relapse during and after tapering is significant and many patients who complete tapering from opioid medication continue to need support, especially during the first 3 to 12 months.⁷ Therefore, if the patient has previously used naloxone, then the post limit quantity for approval will allow for 4 cartons (8 auto-injectors or 8 nasal sprays) of Evzio or Narcan nasal spray (naloxone nasal spray).

REFERENCES

CRITERIA FOR APPROVAL

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Is the requested drug being prescribed in the event that emergency treatment of opioid overdose may be needed? Yes No</td>
</tr>
<tr>
<td>2</td>
<td>Does the patient require more than 2 cartons (4 auto-injectors) of Evzio or 2 cartons (4 nasal sprays) of Narcan nasal spray (naloxone nasal spray) in a 6 month period due to any of the following: A) The type of opioid that the patient is taking (e.g., buprenorphine, pentazocine, long-acting/extended-release opioids), B) The patient is living in an area that has a longer wait time for emergency medical assistance, C) The patient had an overdose episode that required the use of naloxone or the requested drug? [Note: An initial quantity of 2 cartons per 6 months of Evzio or Narcan nasal spray (naloxone nasal spray) will be covered without prior authorization.] [If no, then no further questions.] Yes No</td>
</tr>
<tr>
<td>3</td>
<td>Does the patient require more than the plan allowance of 4 cartons (8 auto-injectors or 8 nasal sprays) per 6 months? Yes No</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mapping Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>1. Go to 2</td>
</tr>
<tr>
<td>You do not meet the requirements of your plan. Your plan covers additional quantities this drug if you may need urgent opioid overdose treatment. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]</td>
</tr>
<tr>
<td>2. Go to 3</td>
</tr>
<tr>
<td>You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when you meet any of these conditions: - You are taking a certain type of opioid (examples are buprenorphine, pentazocine, long-acting/extended-release) - You live in an area that has longer wait time for emergency medical assistance - You had an overdose episode that required the use of naloxone or the requested drug Your request has been denied based on the information we have. [Short Description: Over max quantity and patient does not meet requirements for additional quantities]</td>
</tr>
<tr>
<td>Deny</td>
</tr>
<tr>
<td>------</td>
</tr>
<tr>
<td>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 4 cartons (8 auto-injectors) of Evzio in a 6 month period - 4 cartons (8 nasal sprays) of Narcan nasal spray (naloxone nasal spray) in a 6 month period You have been approved for the maximum quantity that your plan covers for a duration of 6 months. Your request for additional quantities of the requested drug and strength has been denied.</td>
</tr>
</tbody>
</table>

*The 1 month, 3 month, retail, and mail limits will be the same.
SPECIALTY GUIDELINE MANAGEMENT

EXONDYS 51 (eteplirsen)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Exondys 51 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping.

This indication is approved under accelerated approval based on an increase in dystrophin in skeletal muscle observed in some patients treated with Exondys 51. A clinical benefit of Exondys 51 has not been established. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials.

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
Laboratory confirmation of DMD diagnosis with a DMD gene mutation that is amenable to exon 51 skipping (refer to examples in Appendix)

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a physician who specializes in treatment of DMD.

IV. CRITERIA FOR INITIAL APPROVAL

Duchenne Muscular Dystrophy
Authorization of 6 months may be granted for treatment of DMD when all of the following criteria are met:
1. Genetic testing was conducted to confirm the diagnosis of DMD and to identify the specific type of DMD gene mutation.
2. The DMD gene mutation is amenable to exon 51 skipping (refer to examples in Appendix).
3. Treatment with Exondys 51 is initiated before the age of 14.
4. Member is able to achieve an average distance of at least 180 meters while walking independently over 6 minutes.

V. CONTINUATION OF THERAPY
Authorization of 12 months may be granted for members requesting continuation of therapy when the member has demonstrated a response to therapy as evidenced by remaining ambulatory (e.g., able to walk with or without assistance, not wheelchair dependent).

VI. APPENDIX

Examples of DMD gene mutations (exon deletions) amenable to exon 51 skipping
1. Deletion of exon 50
2. Deletion of exon 52
3. Deletion of exons 45-50
4. Deletion of exons 47-50
5. Deletion of exons 48-50
6. Deletion of exons 49-50

VII. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

EYLEA (aflibercept)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Neovascular (wet) age-related macular degeneration
B. Macular edema following retinal vein occlusion
C. Diabetic macular edema
D. Diabetic retinopathy

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Diabetic Macular Edema
Authorization of 24 months may be granted for treatment of diabetic macular edema.

B. Neovascular (Wet) Age-Related Macular Degeneration
Authorization of 24 months may be granted for treatment of neovascular (wet) age-related macular degeneration.

C. Macular Edema Following Retinal Vein Occlusion
Authorization of 24 months may be granted for treatment of macular edema following retinal vein occlusion.

D. Diabetic Retinopathy
Authorization of 24 months may be granted for treatment of diabetic retinopathy.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

FABRAZYME (agalsidase beta)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Fabrazyme is indicated for use in patients with Fabry disease. Fabrazyme reduces globotriaosylceramide (GL-3) deposition in capillary endothelium of the kidney and certain other cell types.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Fabry disease
Indefinite authorization may be granted for treatment of Fabry disease when the diagnosis of Fabry disease was confirmed by enzyme assay demonstrating a deficiency of alpha-galactosidase enzyme activity or by genetic testing, or the member is a symptomatic obligate carrier.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

REBINYN (coagulation factor IX [recombinant], glycoPEGylated)

IDELVION (coagulation factor IX [recombinant], albumin fusion protein)

ALPROLIX (coagulation factor IX [recombinant], Fc fusion protein)

BENEFIX, IXINITY, RIXUBIS (coagulation factor IX [recombinant])

ALPHANINE SD, MONONINE (coagulation factor IX [human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Hemophilia B

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Hemophilia B

Indefinite authorization may be granted for treatment of hemophilia B.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

7. Idelvion [package insert]. Kankakee, IL: CSL Behring LLC; May 2018
SPECIALTY GUIDELINE MANAGEMENT

BEBULIN, PROFILNINE
(factor IX complex [human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
   Hemophilia B

B. Compendial Uses
   1. Bleeding due to low levels of liver-dependent coagulation factors
   2. Factor X deficiency (Bebulin only)
   3. Factor II deficiency (Profilnine only)

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

1. Hemophilia B
   Indefinite authorization may be granted for treatment of hemophilia B.

2. Bleeding Due to Low Levels of Liver-dependent Coagulation Factors
   Indefinite authorization may be granted for treatment of bleeding due to low levels of liver-dependent coagulation factors.

3. Factor X Deficiency
   Indefinite authorization of Bebulin may be granted for treatment of factor X deficiency.

4. Factor II Deficiency
   Indefinite authorization of Profilnine may be granted for treatment of factor II deficiency.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

FACTOR VIII CONCENTRATES

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

Table: Factor VIII Concentrates and Covered Uses

<table>
<thead>
<tr>
<th>Brand</th>
<th>Generic</th>
<th>FDA-Approved Indication(s)</th>
<th>Compendial Indication(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Recombinant Factor VIII Concentrates</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Advate</td>
<td>antihemophilic factor [recombinant]</td>
<td>Hemophilia A</td>
<td>Acquired Hemophilia A</td>
</tr>
<tr>
<td>Afstyla</td>
<td>antihemophilic factor [recombinant], single chain</td>
<td>Hemophilia A</td>
<td></td>
</tr>
<tr>
<td>Helixate FS</td>
<td>antihemophilic factor [recombinant]</td>
<td>Hemophilia A</td>
<td>Acquired Hemophilia A</td>
</tr>
<tr>
<td>Kogenate FS</td>
<td>antihemophilic factor [recombinant]</td>
<td>Hemophilia A</td>
<td>Acquired Hemophilia A</td>
</tr>
<tr>
<td>Kovaltry</td>
<td>antihemophilic factor [recombinant]</td>
<td>Hemophilia A</td>
<td></td>
</tr>
<tr>
<td>Novoeight</td>
<td>antihemophilic factor [recombinant]</td>
<td>Hemophilia A</td>
<td></td>
</tr>
<tr>
<td>Nuwiq</td>
<td>antihemophilic factor [recombinant]</td>
<td>Hemophilia A</td>
<td></td>
</tr>
<tr>
<td>Recombinate</td>
<td>antihemophilic factor [recombinant]</td>
<td>Hemophilia A</td>
<td>Acquired Hemophilia A</td>
</tr>
<tr>
<td>Xyntha</td>
<td>antihemophilic factor [recombinant]</td>
<td>Hemophilia A</td>
<td>Acquired Hemophilia A</td>
</tr>
<tr>
<td></td>
<td><strong>Extended Half-life Recombinant Factor VIII Concentrate</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adynovate</td>
<td>antihemophilic factor [recombinant], PEGylated</td>
<td>Hemophilia A</td>
<td></td>
</tr>
<tr>
<td>Eloctate</td>
<td>antihemophilic factor [recombinant], Fc fusion protein</td>
<td>Hemophilia A</td>
<td></td>
</tr>
<tr>
<td>Jivi</td>
<td>antihemophilic factor [recombinant], PEGylated-aucl</td>
<td>Hemophilia A</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Human Plasma-Derived Factor VIII Concentrates</strong></td>
<td></td>
<td></td>
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<tr>
<td>Hemofil M</td>
<td>antihemophilic factor [human] monoclonal antibody purified</td>
<td>Hemophilia A</td>
<td>Acquired Hemophilia A</td>
</tr>
<tr>
<td>Monoclate-P</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td><strong>Human Plasma-Derived Factor VIII Concentrates That Contain Von Willebrand Factor</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Humate-P</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
All other indications are considered experimental/investigational and are not a covered benefit.

CRITERIA FOR INITIAL APPROVAL

A. Hemophilia A
   Indefinite authorization of Advate, Adynovate, Afstyla, Alphanate, Eloctate, Helixate FS, Hemofil M, Humate-P, Koate, Kogenate FS, Kovaltry, Monoclate-P, Novoeight, Nuwiq, Recombinate or Xyntha may be granted for treatment of hemophilia A when either of the following criteria is met:
   1. Member has mild disease (see Appendix A) and has had an insufficient response to desmopressin or a documented clinical reason for not using desmopressin (see Appendix B).
   2. Member has moderate or severe disease (see Appendix A).

   Indefinite authorization of Jivi may be granted for treatment of hemophilia A when both of the following criteria are met:
   1. Member has previously received treatment for hemophilia A with a factor VIII product.
   2. Member is ≥ 12 years of age.

B. Von Willebrand Disease
   Indefinite authorization of Alphanate, Humate-P or Koate may be granted for treatment of vWD when any of the following criteria is met:
   1. Member has type 1, 2A, 2M, or 2N vWD and has had an insufficient response to desmopressin or a documented clinical reason for not using desmopressin (see Appendix B).
   2. Member has type 2B or type 3 vWD.

C. Acquired Hemophilia A
   Indefinite authorization of Advate, Alphanate, Helixate FS, Hemofil M, Humate-P, Koate, Kogenate FS, Monoclate-P, Recombinate or Xyntha may be granted for treatment of acquired hemophilia A.

D. Acquired von Willebrand Syndrome
   Indefinite authorization of Alphanate or Humate-P may be granted for treatment of acquired von Willebrand syndrome.

II. CONTINUATION OF THERAPY

   All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

III. APPENDICES
Appendix A: Classification of Hemophilia by Clotting Factor Level (% Activity) and Bleeding Episodes

<table>
<thead>
<tr>
<th>Severity</th>
<th>Clotting Factor Level % activity*</th>
<th>Bleeding Episodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe</td>
<td>&lt;1%</td>
<td>Spontaneous bleeding episodes, predominantly into joints and muscles</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Severe bleeding with trauma, injury or surgery</td>
</tr>
<tr>
<td>Moderate</td>
<td>1% to 5%</td>
<td>Occasional spontaneous bleeding episodes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Severe bleeding with trauma, injury or surgery</td>
</tr>
<tr>
<td>Mild</td>
<td>6% to 40%</td>
<td>Severe bleeding with serious injury, trauma or surgery</td>
</tr>
</tbody>
</table>

*Factor assay levels are required to determine the diagnosis and are of value in monitoring treatment response.

Appendix B: Clinical Reasons For Not Utilizing Desmopressin in Patients with Hemophilia A and Type 1, 2A, 2N and 2M WWD

A. Age < 2 years
B. Pregnancy
C. Fluid/electrolyte imbalance
D. High risk for cardiovascular or cerebrovascular disease (especially the elderly)
E. Predisposition to thrombus formation
F. Trauma requiring surgery
G. Life-threatening bleed
H. Contraindication or intolerance to desmopressin
I. Severe type 1 von Willebrand disease

IV. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

FARYDAK (panobinostat)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Farydak, in combination with bortezomib and dexamethasone, is indicated for the treatment of patients with multiple myeloma who have received at least 2 prior regimens, including bortezomib and an immunomodulatory agent. This indication is approved under accelerated approval based on progression free survival. Continued approval of this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

B. Compendial Use

In combination with carfilzomib or in combination with dexamethasone and lenalidomide for the treatment of multiple myeloma in patients who have received at least 2 prior regimens, including bortezomib and an immunomodulatory agent.

All other indications are considered experimental/investigational and are not covered benefits.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for the treatment of multiple myeloma when the member has received at least two prior regimens, including bortezomib and an immunomodulatory agent (“eg.,” lenalidomide, thalidomide, pomalidomide).

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

FARYDAK (panobinostat)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Farydak, in combination with bortezomib and dexamethasone, is indicated for the treatment of patients with multiple myeloma who have received at least 2 prior regimens, including bortezomib and an immunomodulatory agent. This indication is approved under accelerated approval based on progression free survival. Continued approval of this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

B. Compendial Uses

In combination with carfilzomib or in combination with dexamethasone and lenalidomide or in combination with dexamethasone and bortezomib for previously treated multiple myeloma for relapsed or progressive disease in patients who have received at least 2 prior regimens, including bortezomib and an immunomodulatory agent.

All other indications are considered experimental/investigational and are not covered benefits.

II. CRITERIA FOR INITIAL APPROVAL

Multiple Myeloma

Authorization of 12 months may be granted for the treatment of multiple myeloma when the member has received at least two prior regimens, including bortezomib and an immunomodulatory agent (e.g., lenalidomide, thalidomide, pomalidomide).

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

FASENRA (benralizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Fasenra is indicated for the add-on maintenance treatment of patients with severe asthma aged 12 years and older, and with an eosinophilic phenotype.

Limitations of Use:
- Not for treatment of other eosinophilic conditions
- Not for relief of acute bronchospasm or status asthmaticus

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Member’s chart or medical record showing baseline eosinophil level (initial request only)

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 6 months may be granted for treatment of asthma when all of the following criteria are met:
A. Member is 12 years of age or older.
B. Member has a baseline blood eosinophil count of at least 150 cells per microliter.
C. Member has inadequate asthma control (e.g., hospitalization or emergency medical care visit within the past year) despite current treatment with both of the following medications at optimized doses:
   1. Inhaled corticosteroid
   2. Additional controller (long acting beta2-agonist, leukotriene modifier, or sustained-release theophylline)
D. Member will not use Fasenra as monotherapy.
E. Member will not use Fasenra concomitantly with other biologics (e.g., Cinqair, Dupixent, Nucala, Xolair).

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for treatment of asthma when all of the following criteria are met:
A. Member is 12 years of age or older.
B. Asthma control has improved on Fasenra treatment as demonstrated by at least one of the following:
   1. A reduction in the frequency and/or severity of symptoms and exacerbations
   2. A reduction in the daily maintenance oral corticosteroid dose
C. Member will not use Fasenra as monotherapy.
D. Member will not use Fasenra concomitantly with other biologics (e.g., Cinqair, Dupixent, Nucala, Xolair).

V. OTHER

Note: If the member is a current smoker, they should be counseled on the harmful effects of smoking on pulmonary conditions and available smoking cessation options.

VI. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

FEIBA (anti-inhibitor coagulant complex [human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
   Hemophilia A and hemophilia B with inhibitors

B. Compendial Use
   Acquired hemophilia A

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Hemophilia A with Inhibitors
   Indefinite authorization may be granted for treatment of hemophilia A with inhibitors (see Appendix) when the inhibitor titer is $\geq 5$ Bethesda units per milliliter (BU/mL) or if the patient has a history of an inhibitor titer $\geq 5$ BU.

B. Hemophilia B with Inhibitors
   Indefinite authorization may be granted for treatment of hemophilia B with inhibitors (see Appendix) when the inhibitor titer is $\geq 5$ Bethesda units per milliliter (BU/mL) or if the patient has a history of an inhibitor titer $\geq 5$ BU.

C. Acquired Hemophilia A
   Indefinite authorization may be granted for treatment of acquired hemophilia A.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. APPENDIX

Appendix: Inhibitors - Bethesda Units (BU)

The presence of inhibitors is confirmed by a specific blood test called the Bethesda inhibitor assay.
• High-titer inhibitors:
  - > 5 BU/mL
  - Inhibitors act strongly and quickly neutralize factor

• Low-titer inhibitors:
  - < 5 BU/mL
  - Inhibitors act weakly and slowly neutralize factor

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

FERRIPROX (deferiprone)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Transfusional iron overload due to thalassemia syndromes when current chelation therapy is inadequate

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Initial requests: pretreatment serum ferritin level
B. Continuation requests: current serum ferritin level

III. CRITERIA FOR INITIAL APPROVAL

Transfusional Iron Overload
Authorization of 6 months may be granted for treatment of transfusional iron overload due to thalassemia syndromes when both of the following criteria are met:
A. Pretreatment serum ferritin level is consistently greater than 1000 mcg/L.
B. Dose of Ferriprox will not exceed 99 mg/kg per day.

IV. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when both of the following criteria are met:
A. Member is experiencing benefit from therapy as evidenced by a decrease in serum ferritin levels as compared to pretreatment baseline.
B. Serum ferritin level is not consistently below 500 mcg/L.

V. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

FIRDAPSE (amifampridine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Firdapse is indicated for the treatment of Lambert-Eaton myasthenic syndrome (LEMS) in adults.

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of either of the following diagnostic tests is necessary to initiate prior authorization review:

A. Neurophysiology studies (e.g., electromyography)
B. Anti-P/Q type voltage-gated calcium channel antibody test

III. EXCLUSIONS

Coverage will not be provided for members with a history of seizures.

IV. CRITERIA FOR INITIAL APPROVAL

Lambert-Eaton Myasthenic Syndrome (LEMS)

Authorization of 6 months may be granted for treatment of Lambert-Eaton myasthenic syndrome (LEMS) when the diagnosis is confirmed by either of the following:

A. Neurophysiology studies (e.g., electromyography)
B. A positive anti-P/Q type voltage-gated calcium channel antibody test

V. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

VI. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

Firmagon (degarelix)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Firmagon is indicated for the treatment of advanced prostate cancer.

B. Compendial Uses

Prostate cancer

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of prostate cancer.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

FOLLISTIM AQ (follitropin beta injection)
GONAL-F (follitropin alfa injection)
*Hereafter, follitropin will be used to describe all products

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Follistim AQ is indicated for:
1. Induction of ovulation and pregnancy in anovulatory infertile women in whom the cause of infertility is functional and not due to primary ovarian failure
2. Development of multiple follicles in ovulatory women participating in an assisted reproductive technology (ART) program
3. Pregnancy in normal ovulatory women undergoing controlled ovarian stimulation as part of an in vitro fertilization or intracytoplasmic sperm injection (ICSI) cycle
4. Induction of spermatogenesis in men with primary and secondary hypogonadotropic hypogonadism in whom the cause of infertility is not due to primary testicular failure

Gonal-f is indicated for:
1. Induction of ovulation and pregnancy in oligo-anovulatory women in whom the cause of infertility is functional and not due to primary ovarian failure.
2. Development of multiple follicles in ovulatory women as part of an ART cycle.
3. Induction of spermatogenesis in men with primary and secondary hypogonadotropic hypogonadism in whom the cause of infertility is not due to primary testicular failure.

All other indications are considered experimental/investigational and are not a covered benefit.

II. MEDICAL BENEFIT ALIGNMENT

Specialty Guideline Management coverage review will be bypassed for drug(s) being requested for a procedure that has been approved under a member’s medical benefit plan. Such members will be exempt from the requirements in Sections IV and V. A medical authorization number and confirmation of the approved procedure(s) will be required.

NOTE: Some plans may opt-out of medical benefit alignment. Members receiving coverage under such plans must meet the requirements in Sections IV and V.
III. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review for hypogonadotropic hypogonadism: testosterone, FSH, and LH levels.

IV. CRITERIA FOR INITIAL APPROVAL

A. Follicle stimulation

Authorization of 12 months may be granted for members undergoing ovulation induction or assisted reproductive technology (ART) who meet any of the following criteria:
1. Member has completed three or more previous cycles of clomiphene, or
2. Member has a risk factor for poor ovarian response to clomiphene, or
3. Member has a contraindication or exclusion to clomiphene, or
4. Member is 37 years of age or older

B. Hypogonadotropic hypogonadism

Authorization of 12 months may be granted for treatment of hypogonadotropic hypogonadism in members who meet both of the following criteria:
1. Low pretreatment testosterone levels
2. Low or low-normal follicle stimulating hormone (FSH) or luteinizing hormone (LH) levels

V. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

VI. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

FOLOTYN (pralatrexate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   Treatment of patients with relapsed or refractory peripheral T-cell lymphoma (PTCL)

B. Compendial Uses
   1. Adult T-cell leukemia/lymphoma (ATLL)
   2. Mycosis fungoides/Sezary syndrome (MF/SS)
   3. Primary cutaneous CD30+ T-cell lymphoproliferative disorders: cutaneous anaplastic large cell lymphoma (ALCL)
   4. Extranodal NK/T-cell lymphoma, nasal type
   5. Hepatosplenic gamma-delta T-cell lymphoma

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Peripheral T-cell lymphoma (PTCL)
   Authorization of 12 months may be granted for treatment of PTCL when used for relapsed or refractory disease.

B. Adult T-cell leukemia/lymphoma (ATLL)
   Authorization of 12 months may be granted for treatment of ATLL when both of the following criteria are met:
   1. Folotyn is used as a single agent.
   2. Folotyn is used as second-line or subsequent therapy.

C. Mycosis fungoides/Sezary syndrome (MF/SS)
   Authorization of 12 months may be granted for treatment of MF or SS.

D. Primary cutaneous CD30+ T-cell lymphoproliferative disorders
   Authorization of 12 months may be granted for treatment of cutaneous anaplastic large cell lymphoma (ALCL) when Folotyn is used as a single agent.

E. Extranodal NK/T-cell lymphoma, nasal type
   Authorization of 12 months may be granted for treatment of extranodal NK/T-cell lymphoma, nasal type when all of the following criteria are met:
   1. Folotyn will be used as a single agent.
2. Patient has relapsed or refractory disease.
3. Patient has had an inadequate response or contraindication to asparaginase-based therapy (e.g., pegasparagase).

F. Hepatosplenic Gamma-Delta T-cell lymphoma
Authorization of 12 months may be granted for treatment of hepatosplenic gamma-delta T-cell lymphoma when both of the following criteria are met:
1. Folotyn will be used a single agent.
2. The patient has had two or more previous lines of chemotherapy.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

FORTEO (teriparatide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
A. Treatment of postmenopausal women with osteoporosis at high risk for fracture
B. Increase of bone mass in men with primary or hypogonadal osteoporosis at high risk for fracture
C. Treatment of men and women with glucocorticoid-induced osteoporosis at high risk for fracture

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Supporting chart notes or medical record indicating a history of fractures, T-score, and FRAX fracture probability as applicable to Section III.

III. CRITERIA FOR INITIAL APPROVAL

A. Postmenopausal osteoporosis

Authorization of a lifetime total of 24 months for parathyroid hormone analogs (e.g., abaloparatide or teriparatide) may be granted to postmenopausal members with osteoporosis when ANY of the following criteria are met:

1. Member has a history of fragility fractures
2. Member has a pre-treatment T-score less than or equal to -2.5 OR member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B) and meets ANY of the following criteria:
   a. Member has indicators of higher fracture risk (e.g., advanced age, frailty, glucocorticoid use, very low T-scores [less than or equal to -3.5], or increased fall risk)
   b. Member has failed prior treatment with or is intolerant to previous injectable osteoporosis therapy (e.g., zoledronic acid [Reclast], denosumab [Prolia])
   c. Member has had an oral bisphosphonate trial of at least 1-year duration or there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)

B. Primary or hypogonadal osteoporosis in men

Authorization of a lifetime total of 24 months for parathyroid hormone analogs (e.g., abaloparatide or teriparatide) may be granted to male members with primary or hypogonadal osteoporosis when ANY of the following criteria are met:
1. Member has a history of an osteoporotic vertebral or hip fracture
2. Member meets criteria BOTH of the following criteria:
   a. Member has a pre-treatment T-score less than or equal to -2.5 OR member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B)
   b. Member has had an oral bisphosphonate trial of at least 1-year duration OR there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)

C. Glucocorticoid-induced Osteoporosis
Authorization of a lifetime total of 24 months for parathyroid hormone analogs (e.g., abaloparatide or teriparatide) may be granted for members with glucocorticoid-induced osteoporosis when ALL of the following criteria are met:
1. Member has had an oral bisphosphonate trial of at least 1-year duration OR there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)
2. Member is currently receiving or will be initiating glucocorticoid therapy
3. Member meets ANY of the following criteria:
   a. Member has a history of a fragility fracture
   b. Member has a pre-treatment T-score less than or equal to -2.5
   c. Member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B)

IV. CONTINUATION OF THERAPY
All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria AND have received less than 24 months of total lifetime therapy with parathyroid hormone analogs (e.g., abaloparatide or teriparatide).

V. APPENDIX
Appendix A. Clinical reasons to avoid oral bisphosphonate therapy
- Esophageal abnormality that delays emptying such as stricture of achalasia
- Active upper gastrointestinal problem (e.g., dysphagia, gastritis, duodenitis, erosive esophagitis, ulcers)
- Inability to stand or sit upright for at least 30 to 60 minutes
- Inability to take at least 30 to 60 minutes before first food, drink, or medication of the day
- Renal insufficiency (creatinine clearance < 35 mL/min)
- History of intolerance to an oral bisphosphonate

Appendix B. WHO Fracture Risk Assessment Tool
- High FRAX fracture probability: 10 year major osteoporotic fracture risk ≥ 20% or hip fracture risk ≥ 3%.
- 10-year probability; calculation tool available at: https://www.sheffield.ac.uk/FRAX/
- The estimated risk score generated with FRAX should be multiplied by 1.15 for major osteoporotic fracture and 1.2 for hip fracture if glucocorticoid treatment is greater than 7.5 mg per day.

VI. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

GALAFOLD (migalastat)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Galafold is indicated for the treatment of adults with a confirmed diagnosis of Fabry disease and an amenable galactosidase alpha gene (GLA) variant based on in vitro assay data.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Fabry disease with an amenable galactosidase alpha gene (GLA) variant
Indefinite authorization may be granted for treatment of Fabry disease with an amenable galactosidase alpha gene (GLA) variant when all of the following criteria are met:
A. The diagnosis of Fabry disease was confirmed by enzyme assay demonstrating a deficiency of alpha-galactosidase enzyme activity or by genetic testing, or the member is a symptomatic obligate carrier.
B. Member has an amenable galactosidase alpha gene (GLA) variant based on in vitro assay data.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

Intramuscular Immune Globulin:
GamaSTAN® S/D (Immune Globulin [Human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
A. Pre- or post-exposure prophylaxis of hepatitis A
B. Postexposure prophylaxis/modification of measles (rubeola) in susceptible persons
C. Postexposure prophylaxis of varicella in immunosuppressed patients when varicella-zoster immune globulin is not available
D. Postexposure prophylaxis of rubella during pregnancy

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 1 month may be granted when GamaSTAN SD is used in one of the following clinical settings:
A. Prophylaxis of hepatitis A
B. Prophylaxis of measles (rubeola)
C. Prophylaxis of varicella
D. Prophylaxis of rubella

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

GAMIFANT (emapalumab-lzsg)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Gamifant is indicated for the treatment of adult and pediatric (newborn and older) patients with primary hemophagocytic lymphohistiocytosis (HLH) with refractory, recurrent or progressive disease or intolerance with conventional HLH therapy.

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review: medical record documentation (i.e., chart notes or laboratory report) confirming the diagnosis of HLH with the presence of the following: A) a mutation in one of the genes listed under III.B.1 or B) clinical signs and symptoms listed under III.B.2.

III. CRITERIA FOR INITIAL APPROVAL

Primary HLH

Authorization of 12 months may be granted for treatment of primary HLH when all of the following criteria are met:

A. Member has refractory, recurrent or progressive disease or intolerance with conventional HLH therapy.

B. Member’s diagnosis of primary HLH was confirmed by either of the following:
   1. Mutation in one of the following genes: PRF1, UNC13D, STX11 and STXBP2
   2. Presence of at least 5 of the following:
      a. Fever
      b. Splenomegaly
      c. Cytopenias (affecting at least 2 of 3 lineages in the peripheral blood: hemoglobin less than 9 g/dL [hemoglobin less than 10 g/dL in infants younger than 4 weeks], platelets less than 100,000/microliter, neutrophils less than 1,000/microliter)
      d. Hypertriglyceridemia (fasting triglyceride greater than 265 mg/dL) or hypofibrinogenemia (less than 150 mg/dL)
      e. Hemophagocytosis in bone marrow or spleen or lymph nodes or liver
      f. Low or absent natural killer (NK) cell activity
      g. Ferritin greater than 500 ng/mL
      h. Soluble CD25 (soluble IL-2 receptor alpha) level above 2400 U/mL, or above age-adjusted, laboratory-specific normal levels (defined as 2 standard deviation from the mean)

C. Possible causes of secondary or acquired forms of HLH (e.g., autoimmune disease, persistent infection, malignancy, or loss of inhibitory immune mechanisms) have been ruled out.
D. Member has been evaluated for tuberculosis (TB) risk factors and has undergone pretreatment screening for latent TB with the purified protein derivative (PPD) skin test or interferon gamma release assay. 
E. If member has a positive test result or is at risk for TB, prophylactic treatment for TB must be initiated before starting therapy.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

GATTEX (teduglutide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Gattex is indicated for the treatment of adult patients with short bowel syndrome (SBS) who are dependent on parenteral support.

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review:

A. For initial authorization: chart notes supporting the use of parenteral nutrition/IV fluids for 12 months and current volume of parenteral support in liters per week

B. For continuation of treatment for patients currently on parenteral nutrition: chart notes supporting the continued use of parenteral nutrition/IV fluids and current volume of parenteral support in liters per week

C. For continuation of treatment for patients who were previously on parenteral nutrition and have been weaned off parenteral nutrition/IV fluids while on Gattex therapy: chart notes supporting the volume of parenteral support in liters per week required at baseline.

III. CRITERIA FOR INITIAL APPROVAL

Short bowel syndrome (SBS) 1-3

Authorization of 6 months may be granted for treatment of short bowel syndrome in members who have been dependent on parenteral nutrition and/or intravenous fluids for at least 12 months.

IV. CONTINUATION OF THERAPY

Short bowel syndrome (SBS) 1-3

Authorization of 6 months may be granted for treatment of short bowel syndrome in members who meet either of the following:

A. Patient remains dependent on parenteral nutrition and/or intravenous fluids and whose requirement for parenteral support has decreased by at least 20% from baseline while on Gattex therapy.

B. Patient who was previously dependent on parenteral nutrition and/or intravenous fluids and has been able to wean off the requirement for parenteral support while on Gattex therapy.
V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

GAZYVA (obinutuzumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Chronic Lymphocytic Leukemia (CLL)
      Gazyva, in combination with chlorambucil, is indicated for the treatment of patients with previously untreated CLL.
   2. Follicular Lymphoma
      a. Gazyva, in combination with bendamustine followed by Gazyva monotherapy, is indicated for the treatment of patients with follicular lymphoma who relapsed after, or are refractory to, a rituximab-containing regimen.
      b. Gazyva, in combination with chemotherapy followed by Gazyva monotherapy in patients achieving at least a partial remission, is indicated for the treatment of adult patients with previously untreated stage II bulky, III or IV follicular lymphoma.

B. Compendial Uses
   1. Chronic lymphocytic leukemia, relapsed or refractory disease
   2. Small lymphocytic lymphoma (SLL) (managed in the same manner as CLL)
   3. Gastric MALT lymphoma, recurrent or progressive disease
   4. Non-gastric MALT lymphoma, refractory or progressive disease
   5. Nodal and splenic marginal zone lymphoma, refractory or progressive disease
   6. Primary cutaneous B-cell lymphomas: primary cutaneous marginal zone or follicle center lymphoma

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Chronic Lymphocytic Leukemia (CLL) and Small Lymphocytic Lymphoma (SLL)
   Authorization of 12 months may be granted for the treatment of CD20-positive CLL/SLL.

B. Follicular Lymphoma
   Authorization of 30 months total may be granted for the treatment of CD20-positive follicular lymphoma.

C. Gastric MALT Lymphoma, Non-gastric MALT Lymphoma, Nodal and Splenic Marginal Zone Lymphoma
   Authorization of 30 months total may be granted for the treatment of recurrent, refractory, or progressive CD20-positive gastric MALT lymphoma, non-gastric MALT lymphoma, nodal marginal zone lymphoma, or splenic marginal zone lymphoma.
D. Primary Cutaneous Marginal Zone or Follicle Center Lymphoma
Authorization of 30 months total may be granted for the treatment of CD20-positive primary cutaneous marginal zone or follicle center lymphoma.

III. CONTINUATION OF THERAPY
All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

Gemzar (gemcitabine)
gemcitabine (generic)

POLICY

A. INDICATIONS
The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
1. In combination with carboplatin for the treatment of patients with advanced ovarian cancer that has relapsed at least 6 months after completion of platinum-based therapy
2. In combination with paclitaxel for the first-line treatment of patients with metastatic breast cancer after failure of prior anthracycline-containing adjuvant chemotherapy, unless anthracyclines were clinically contraindicated
3. In combination with cisplatin for the first-line treatment of patients with inoperable, locally advanced (Stage IIIA or IIIB), or metastatic (Stage IV) non-small cell lung cancer
4. As first-line treatment for patients with locally advanced (nonresectable Stage II or Stage III) or metastatic (Stage IV) adenocarcinoma of the pancreas. Gemcitabine is indicated for patients previously treated with 5-FU.

Compendial Uses
1. Bladder cancer, primary carcinoma of the urethra, upper genitourinary tract tumors, urothelial carcinoma of the prostate, non-urothelial and urothelial cancer with variant histology
2. Bone cancer
   • Ewing's sarcoma family of tumors
   • osteosarcoma
3. Breast cancer
4. Head and neck cancers
   • nasopharyngeal cancer
5. Hepatobiliary cancers
   • extrahepatic cholangiocarcinoma
   • gallbladder cancer
   • intrahepatic cholangiocarcinoma
6. Hodgkin lymphoma
7. Kidney cancer
8. Malignant pleural mesothelioma
9. Non-Hodgkin's lymphoma
10. Non-small cell lung cancer (NSCLC)
11. Occult primary
12. Epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer
13. Pancreatic adenocarcinoma
14. Small cell lung cancer (SCLC)
15. Soft tissue sarcoma (STS)
16. Testicular cancer
17. Thymomas/thymic carcinomas
18. Uterine sarcoma
19. AIDS-Related Kaposi Sarcoma

All other indications are considered experimental/investigational and are not a covered benefit.

B. CRITERIA FOR INITIAL APPROVAL

1. Pancreatic Adenocarcinoma
   Authorization of 12 months may be granted for the treatment of pancreatic adenocarcinoma.

2. Breast Cancer
   Authorization of 12 months may be granted for the treatment of recurrent or metastatic breast cancer.

3. Intrahepatic and Extrahepatic Cholangiocarcinoma and Gallbladder Cancer
   Authorization of 12 months may be granted for the treatment of intrahepatic and extrahepatic cholangiocarcinoma and gallbladder cancer.

4. Epithelial Ovarian Cancer, Fallopian Tube Cancer, Primary Peritoneal Cancer
   Authorization of 12 months may be granted for the treatment of epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer.

5. Non-Small Cell Lung Cancer (NSCLC)
   Authorization of 12 months may be granted for the treatment of NSCLC.

6. Bladder Cancer, Primary Carcinoma of the Urethra, Upper Genitourinary Tract Tumors, Urothelial Carcinoma of the Prostate, Non-Urothelial and Urothelial cancer with Variant Histology
   Authorization of 12 months may be granted for the treatment of bladder cancer, primary carcinoma of the urethra, upper genitourinary tract tumors, urothelial carcinoma of the prostate, and non-urothelial and urothelial cancer with variant histology.

7. Small Cell Lung Cancer (SCLC)
   Authorization of 12 months may be granted for the treatment of SCLC.

8. Soft Tissue Sarcoma
   Authorization of 12 months may be granted for the treatment of soft tissue sarcoma.

9. Bone Cancer
   Authorization of 12 months may be granted for the treatment of Ewing’s sarcoma and osteosarcoma.

10. Nasopharyngeal Cancer
    Authorization of 12 months may be granted for the treatment of nasopharyngeal cancer.

11. Hodgkin Lymphoma
    Authorization of 12 months may be granted for the treatment of Hodgkin lymphoma.

12. Kidney Cancer
    Authorization of 12 months may be granted for the treatment of kidney cancer.

13. Malignant Pleural Mesothelioma
Authorization of 12 months may be granted for the treatment of malignant pleural mesothelioma.

14. Non-Hodgkin’s Lymphoma (NHL)
   Authorization of 12 months may be granted for the treatment of NHL.

15. Occult Primary Tumors (cancer of unknown primary)
   Authorization of 12 months may be granted for the treatment of occult primary tumors.

16. Testicular Cancer
   Authorization of 12 months may be granted for the treatment of testicular cancer.

17. Thymomas and Thymic Carcinomas
   Authorization of 12 months may be granted for the treatment of thymomas and thymic carcinomas.

18. Uterine Sarcoma
   Authorization of 12 months may be granted for the treatment of uterine sarcoma.

19. AIDS-Related Kaposi Sarcoma
   Authorization of 12 months may be granted for the treatment of AIDS-Related Kaposi Sarcoma.

C. CONTINUATION OF THERAPY
   All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria.

D. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

GILENYA (fingolimod)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication: Gilenya is indicated for the treatment of relapsing forms of multiple sclerosis (MS) in patients 10 years of age and older.

All other indications are considered experimental/investigational and are not covered benefits.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted to members with a relapsing form of multiple sclerosis who are experiencing disease stability or improvement while receiving Gilenya.

IV. OTHER CRITERIA

Members will not use Gilenya concomitantly with other medications used for the treatment of multiple sclerosis, excluding Ampyra.

V. REFERENCE

SPECIALTY GUIDELINE MANAGEMENT

GILOTRIF (afatinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. EGFR Mutation-Positive, Metastatic Non-Small Cell Lung Cancer
      Gilotrif is indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have non-resistant epidermal growth factor receptor (EGFR) mutations as detected by an FDA-approved test.
   2. Previously Treated, Metastatic Squamous NSCLC
      Gilotrif is indicated for the treatment of patients with metastatic squamous NSCLC progressing after platinum-based chemotherapy.

B. Compendial Uses
   1. NSCLC, recurrent, advanced or metastatic sensitizing EGFR mutation-positive
   2. Recurrent brain metastases from EGFR sensitizing mutation-positive NSCLC
   3. Non-nasopharyngeal head and neck cancer

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: For NSCLC, EGFR mutation testing results (where applicable).

III. CRITERIA FOR INITIAL APPROVAL

A. Non-Small Cell Lung Cancer (NSCLC)
   1. Authorization of 12 months may be granted for treatment of recurrent, advanced or metastatic NSCLC (including brain metastases from NSCLC) when the member has sensitizing EGFR mutation-positive disease.
   2. Authorization of 12 months may be granted for treatment of metastatic squamous NSCLC progressing after platinum-based chemotherapy.

B. Head and Neck Cancer
   Authorization of 12 months may be granted for treatment of non-nasopharyngeal head and neck cancer following disease progression on or after platinum-containing chemotherapy.
IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced an unacceptable toxicity.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

GENOTROPIN (somatropin)
HUMATROPE (somatropin)
NORDITROPIN (somatropin)
NUTROPIN AQ (somatropin)
OMNITROPE (somatropin)
SAIZEN (somatropin)
ZOMACTON (somatropin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no contraindications or exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Pediatric patients with growth failure due to any of the following:
      a. Growth hormone (GH) deficiency
      b. Turner syndrome
      c. Noonan syndrome
      d. Small for gestational age (SGA)
      e. Prader-Willi syndrome
      f. Chronic kidney disease (CKD)
      g. Short stature homeobox-containing gene (SHOX) deficiency
      h. Idiopathic short stature (ISS)*
   2. Adults with childhood-onset or adult-onset GH deficiency

   * ISS may not be covered by some plans

B. Compendial Uses
   1. Human immunodeficiency virus (HIV)-associated wasting/cachexia
   2. Short bowel syndrome (SBS)
   3. Growth failure associated with any of the following:
      a. Cerebral palsy
      b. Congenital adrenal hyperplasia
      c. Cystic fibrosis
      d. Russell-Silver syndrome

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review for both initial and continuation of therapy requests (where applicable):

A. Medical records supporting the diagnosis of neonatal GH deficiency
B. Pretreatment growth hormone provocative test result(s) (laboratory report or medical record documentation)

C. Pretreatment and/or current IGF-1 level (laboratory report or medical record documentation)*

D. The following laboratory test reports must be provided:
   1. Diagnostic karyotype results in Turner syndrome
   2. Diagnostic genetic test results in Prader-Willi syndrome
   3. Diagnostic molecular or genetic test results in SHOX deficiency

E. The following information must be provided for all continuation of therapy requests:
   1. Total duration of treatment (approximate duration is acceptable)
   2. Date of last dose administered
   3. Approving health plan/pharmacy benefit manager
   4. Date of prior authorization/approval
   5. Prior authorization approval letter

* IGF-1 levels vary based on the laboratory performing the analysis. Laboratory-specific values must be provided to determine whether the value is within the normal range.

III. PRESCRIBER SPECIALTIES

For all diagnoses excluding HIV-associated wasting/cachexia, therapy must be prescribed by or in consultation with any of the following specialists:

A. Endocrinologist
B. Pediatric endocrinologist
C. Geneticist
D. Pediatric nephrologist (CKD only)
E. Gastroenterologist/Nutritional support specialist (SBS only)

IV. INITIAL CRITERIA FOR APPROVAL

A. Pediatric GH Deficiency

Authorization of 12 months may be granted to members with pediatric GH deficiency when EITHER criteria 1. or 2. below is met:

1. Member is a neonate or was diagnosed with GH deficiency as a neonate. Medical records must be available to support the diagnosis of neonatal GH deficiency (e.g., hypoglycemia with random GH level, evidence of multiple pituitary hormone deficiency, chart notes, or magnetic resonance imaging [MRI] results).
2. Member meets ALL of the following:
   a. Member has EITHER:
      i. Two pretreatment pharmacologic provocative GH tests with both results demonstrating a peak GH level < 10 ng/mL, OR
      ii. A documented pituitary or CNS disorder (refer to Appendix A) and a pretreatment IGF-1 level > 2 standard deviations (SD) below the mean
   b. For members < 2.5 years of age at initiation of treatment, the pretreatment height is > 2 SD below the mean and growth velocity is slow
   c. For members ≥ 2.5 years of age at initiation of treatment:
      i. Pretreatment height is > 2 SD below the mean and 1-year height velocity is > 1 SD below the mean, OR
      ii. Pretreatment 1-year height velocity is > 2 SD below the mean
   d. Epiphyses are open
B. **Idiopathic Short Stature (may not be covered by some plans)**
Authorization of 12 months may be granted to members with ISS when ALL of the following criteria are met:
1. Pretreatment height is > 2.25 SD below the mean
2. Predicted adult height is < 5’3” for boys and < 4’11” for girls
3. Pediatric GH deficiency has been ruled out with a provocative GH test (peak GH level ≥ 10 ng/mL)
4. Epiphyses are open

C. **Small for Gestational Age**
Authorization of 12 months may be granted to members born SGA when ALL of the following criteria are met:
1. Member meets at least one of the following:
   a. Birth weight < 2500 g at gestational age > 37 weeks
   b. Birth weight or length less than 3rd percentile for gestational age
   c. Birth weight or length ≥ 2 SD below the mean for gestational age
2. Pretreatment age is ≥ 2 years
3. Member failed to manifest catch-up growth by age 2 (i.e., pretreatment height > 2 SD below the mean)
4. Epiphyses are open

D. **Turner Syndrome**
Authorization of 12 months may be granted to members with Turner syndrome when ALL of the following criteria are met:
1. Diagnosis was confirmed by karyotyping
2. Patient’s pretreatment height is less than the 5th percentile for age
3. Epiphyses are open

E. **Growth Failure Associated with Chronic Kidney Disease, Cerebral Palsy, Congenital Adrenal Hyperplasia, Cystic Fibrosis, and Russell-Silver Syndrome**
Authorization of 12 months may be granted to members with CKD, cerebral palsy, congenital adrenal hyperplasia, cystic fibrosis, or Russell-Silver syndrome when ALL of the following criteria are met:
1. For members < 2.5 years of age at initiation of treatment, the pretreatment height is > 2 SD below the mean and growth velocity is slow
2. For members ≥ 2.5 years of age at initiation of treatment:
   a. Pretreatment height is > 2 SD below the mean and 1-year height velocity is > 1 SD below the mean, OR
   b. Pretreatment 1-year height velocity is > 2 SD below the mean
3. Epiphyses are open

F. **Prader-Willi Syndrome**
Authorization of 12 months may be granted to members with Prader-Willi syndrome when the diagnosis was confirmed by genetic testing demonstrating any of the following:
1. Deletion in the chromosomal 15q11.2-q13 region
2. Maternal uniparental disomy in chromosome 15
3. Imprinting defects or translocations involving chromosome 15

G. **Noonan Syndrome**
Authorization of 12 months may be granted to members with Noonan syndrome when ALL of the following criteria are met:
1. Pretreatment height is > 2 SD below the mean and 1-year height velocity is > 1 SD below the mean OR pretreatment 1-year height velocity is > 2 SD below the mean
2. Epiphyses are open
H. Short Stature Homeobox-Containing Gene Deficiency
Authorization of 12 months may be granted to members with SHOX deficiency when ALL of the following criteria are met:
1. The diagnosis of SHOX deficiency was confirmed by molecular or genetic analyses
2. Pretreatment height is > 2 SD below the mean and 1-year height velocity is > 1 SD below the mean OR pretreatment 1-year height velocity is > 2 SD below the mean
3. Epiphyses are open

I. Adult GH Deficiency
Authorization of 12 months may be granted to members with adult GH deficiency when ANY of the following criteria is met:
1. Member has had 2 pretreatment pharmacologic provocative GH tests and both results demonstrated GH levels < 5 ng/mL, unless the agent is Macrilen in which case a GH level of less than 2.8 ng/ml confirms the presence of adult GHD
2. Member has had 1 pretreatment pharmacologic provocative GH test that demonstrated a GH level < 5 ng/mL AND has a pretreatment IGF-1 level that is low for age and gender, unless the agent is Macrilen in which case a GH level of less than 2.8 ng/ml confirms the presence of adult GHD
3. Member has a structural abnormality of the hypothalamus or pituitary (refer to Appendix A) and ≥ 3 documented pituitary hormone deficiencies (refer to Appendix B)
4. Member has childhood-onset GH deficiency and a congenital abnormality of the hypothalamus or pituitary (refer to Appendix A)

J. HIV-Associated Wasting/Cachexia
Authorization of 12 weeks may be granted to members with HIV-associated wasting or cachexia when ALL of the following criteria are met:
1. Member has tried and had a suboptimal response to alternative therapies (e.g., cyproheptadine, dronabinol, megestrol acetate or testosterone if hypogonadal) unless the member has a contraindication or intolerance to alternative therapies
2. Member is currently on antiretroviral therapy
3. Pretreatment BMI is < 18.5 kg/m² (see Appendix C)

K. Short Bowel Syndrome
Authorization of a lifetime total of 8 weeks may be granted to members with short bowel syndrome when GH will be used in conjunction with optimal management of SBS.

V. CONTINUATION OF THERAPY
A. Pediatric GH Deficiency, Turner Syndrome, Noonan Syndrome, CKD, SGA, ISS, SHOX deficiency, Congenital Adrenal Hyperplasia, Cerebral Palsy, Cystic Fibrosis, and Russell-Silver Syndrome
Authorization of 12 months may be granted for continuation of therapy when ALL of the following criteria are met:
1. Epiphyses are open (confirmed by X-ray or X-ray is not available)
2. Member’s growth rate is > 2 cm/year unless there is a documented clinical reason for lack of efficacy (e.g., on treatment less than 1 year, nearing final adult height/late stages of puberty)

B. Prader-Willi Syndrome
Authorization of 12 months may be granted for continuation of therapy when the member’s body composition and psychomotor function have improved or stabilized in response to GH therapy.

C. Adult GH Deficiency
Authorization of 12 months may be granted for continuation of therapy when all criteria for initial authorization are met (refer to Section IV. I. above).

D. HIV-Associated Wasting/Cachexia

Authorization of 12 weeks may be granted for continuation of therapy when ALL of the following criteria are met:
1. Member is currently on antiretroviral therapy.
2. Current BMI is < 27 kg/m² (see Appendix C).

VI. APPENDICES

A. Appendix A: Examples of Hypothalamic/Pituitary/CNS Disorders
1. Congenital genetic abnormalities
   a. Known mutations in growth-hormone-releasing hormone (GHRH) receptor, GH gene, GH receptor, or pituitary transcription factors
2. Congenital structural abnormalities
   a. Optic nerve hypoplasia/septo-optic dysplasia
   b. Agenesis of corpus callosum
   c. Empty sella syndrome
   d. Ectopic posterior pituitary
   e. Pituitary aplasia/hypoplasia
   f. Pituitary stalk defect
   g. Anencephaly or prosencephaly
   h. Other mid-line defects
   i. Vascular malformations
3. Acquired structural abnormalities (or causes of hypothalamic/pituitary damage)
   a. CNS tumors/neoplasms (e.g., craniopharyngioma, glioma, pituitary adenoma)
   b. Cysts ( Rathke cleft cyst or arachnoid cleft cyst)
   c. Surgery
   d. Radiation
   e. Chemotherapy
   f. CNS infections
   g. CNS infarction (e.g., Sheehan’s syndrome)
   h. Inflammatory lesions (e.g., autoimmune hypophysitis)
   i. Infiltrative lesions (e.g., sarcoidosis, histiocytosis)
   j. Head trauma/traumatic brain injury
   k. Aneurysmal subarachnoid hemorrhage

B. Appendix B: Pituitary Hormones (Other than Growth Hormone)
1. Adrenocorticotropic hormone (ACTH)
2. Antidiuretic hormone (ADH)
3. Follicle stimulating hormone (FSH)
4. Luteinizing hormone (LH)
5. Thyroid stimulating hormone (TSH)
6. Prolactin

C. Appendix C: Calculation of BMI

\[
\text{BMI} = \frac{\text{Weight (pounds)} \times 703}{\text{Height (inches)}^2} \quad \text{OR} \quad \frac{\text{Weight (kg)}}{\text{Height (m)}^2}
\]
BMI classification:

- Underweight: $< 18.5 \text{ kg/m}^2$
- Normal weight: $18.5 – 24.9 \text{ kg/m}^2$
- Overweight: $25 – 29.9 \text{ kg/m}^2$
- Obesity (class 1): $30 – 34.9 \text{ kg/m}^2$
- Obesity (class 2): $35 – 39.9 \text{ kg/m}^2$
- Extreme obesity: $\geq 40 \text{ kg/m}^2$

VII. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

GENOTROPIN (somatropin)
HUMATROPE (somatropin)
NORDITROPIN (somatropin)
NUTROPIN AQ (somatropin)
OMNITROPE (somatropin)
SAIZEN (somatropin)
ZOMACTON (somatropin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no contraindications or exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Pediatric patients with growth failure due to any of the following:
      a. Growth hormone (GH) deficiency
      b. Turner syndrome
      c. Noonan syndrome
      d. Small for gestational age (SGA)
      e. Prader-Willi syndrome
      f. Chronic kidney disease (CKD)
      g. Short stature homeobox-containing gene (SHOX) deficiency
   2. Adults with childhood-onset or adult-onset GH deficiency

B. Compendial Uses
   1. Human immunodeficiency virus (HIV)-associated wasting/cachexia
   2. Short bowel syndrome (SBS)
   3. Growth failure associated with any of the following:
      a. Cerebral palsy
      b. Congenital adrenal hyperplasia
      c. Cystic fibrosis
      d. Russell-Silver syndrome

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review for both initial and continuation of therapy requests (where applicable):

A. Medical records supporting the diagnosis of neonatal GH deficiency
B. Pretreatment growth hormone provocative test result(s) (laboratory report or medical record documentation)
C. Pretreatment and/or current IGF-1 level (laboratory report or medical record documentation)*
D. The following laboratory test reports must be provided:
   1. Diagnostic karyotype results in Turner syndrome
   2. Diagnostic genetic test results in Prader-Willi syndrome
   3. Diagnostic molecular or genetic test results in SHOX deficiency
E. The following information must be provided for all continuation of therapy requests:
   1. Total duration of treatment (approximate duration is acceptable)
   2. Date of last dose administered
   3. Approving health plan/pharmacy benefit manager
   4. Date of prior authorization/approval
   5. Prior authorization approval letter

* IGF-1 levels vary based on the laboratory performing the analysis. Laboratory-specific values must be provided to
determine whether the value is within the normal range.

III. PRESCRIBER SPECIALTIES

For all diagnoses excluding HIV-associated wasting/cachexia, therapy must be prescribed by or in consultation
with any of the following specialists:
A. Endocrinologist
B. Pediatric endocrinologist
C. Geneticist
D. Pediatric nephrologist (CKD only)
E. Gastroenterologist/Nutritional support specialist (SBS only)

IV. INITIAL CRITERIA FOR APPROVAL

A. Pediatric GH Deficiency
   Authorization of 12 months may be granted to members with pediatric GH deficiency when EITHER
criteria 1. or 2. below is met:
   1. Member is a neonate or was diagnosed with GH deficiency as a neonate. Medical records must be
      available to support the diagnosis of neonatal GH deficiency (e.g., hypoglycemia with random GH
      level, evidence of multiple pituitary hormone deficiency, chart notes, or magnetic resonance imaging
      [MRI] results).
   2. Member meets ALL of the following:
      a. Member has EITHER:
         i. Two pretreatment pharmacologic provocative GH tests with both results demonstrating a peak
            GH level < 10 ng/mL, OR
         ii. A documented pituitary or CNS disorder (refer to Appendix A) and a pretreatment IGF-1 level
             > 2 standard deviations (SD) below the mean
      b. For members < 2.5 years of age at initiation of treatment, the pretreatment height is > 2 SD below
         the mean and growth velocity is slow
      c. For members ≥ 2.5 years of age at initiation of treatment:
         i. Pretreatment height is > 2 SD below the mean and 1-year height velocity is > 1 SD below the
            mean, OR
         ii. Pretreatment 1-year height velocity is > 2 SD below the mean
      d. Epiphyses are open

B. Small for Gestational Age
   Authorization of 12 months may be granted to members born SGA when ALL of the following criteria are
   met:
1. Member meets at least one of the following:
   a. Birth weight < 2500 g at gestational age > 37 weeks
   b. Birth weight or length less than 3rd percentile for gestational age
   c. Birth weight or length ≥ 2 SD below the mean for gestational age
2. Pretreatment age is ≥ 2 years
3. Member failed to manifest catch-up growth by age 2 (i.e., pretreatment height > 2 SD below the mean)
4. Epiphyses are open

C. Turner Syndrome
Authorization of 12 months may be granted to members with Turner syndrome when ALL of the following criteria are met:
1. Diagnosis was confirmed by karyotyping
2. Patient’s pretreatment height is less than the 5th percentile for age
3. Epiphyses are open

D. Growth Failure Associated with Chronic Kidney Disease, Cerebral Palsy, Congenital Adrenal Hyperplasia, Cystic Fibrosis, and Russell-Silver Syndrome
Authorization of 12 months may be granted to members with CKD, cerebral palsy, congenital adrenal hyperplasia, cystic fibrosis, or Russell-Silver syndrome when ALL of the following criteria are met:
1. For members < 2.5 years of age at initiation of treatment, the pretreatment height is > 2 SD below the mean and growth velocity is slow
2. For members ≥ 2.5 years of age at initiation of treatment:
   a. Pretreatment height is > 2 SD below the mean and 1-year height velocity is > 1 SD below the mean, OR
   b. Pretreatment 1-year height velocity is > 2 SD below the mean
3. Epiphyses are open

E. Prader-Willi Syndrome
Authorization of 12 months may be granted to members with Prader-Willi syndrome when the diagnosis was confirmed by genetic testing demonstrating any of the following:
1. Deletion in the chromosomal 15q11.2-q13 region
2. Maternal uniparental disomy in chromosome 15
3. Imprinting defects or translocations involving chromosome 15

F. Noonan Syndrome
Authorization of 12 months may be granted to members with Noonan syndrome when ALL of the following criteria are met:
1. Pretreatment height is > 2 SD below the mean and 1-year height velocity is > 1 SD below the mean OR pretreatment 1-year height velocity is > 2 SD below the mean
2. Epiphyses are open

G. Short Stature Homeobox-Containing Gene Deficiency
Authorization of 12 months may be granted to members with SHOX deficiency when ALL of the following criteria are met:
1. The diagnosis of SHOX deficiency was confirmed by molecular or genetic analyses
2. Pretreatment height is > 2 SD below the mean and 1-year height velocity is > 1 SD below the mean OR pretreatment 1-year height velocity is > 2 SD below the mean
3. Epiphyses are open

H. Adult GH Deficiency
Authorization of 12 months may be granted to members with adult GH deficiency when ANY of the following criteria is met:
1. Member has had 2 pretreatment pharmacologic provocative GH tests and both results demonstrated GH levels < 5 ng/mL, unless the agent is Macrilen in which case a GH level of less than 2.8 ng/ml confirms the presence of adult GHD
2. Member has had 1 pretreatment pharmacologic provocative GH test that demonstrated a GH level < 5 ng/mL AND has a pretreatment IGF-1 level that is low for age and gender, unless the agent is Macrilen in which case a GH level of less than 2.8 ng/ml confirms the presence of adult GHD
3. Member has a structural abnormality of the hypothalamus or pituitary (refer to Appendix A) and ≥ 3 documented pituitary hormone deficiencies (refer to Appendix B)
4. Member has childhood-onset GH deficiency and a congenital abnormality of the hypothalamus or pituitary (refer to Appendix A)

I. HIV-Associated Wasting/Cachexia
Authorization of 12 weeks may be granted to members with HIV-associated wasting or cachexia when ALL of the following criteria are met:
1. Member has tried and had a suboptimal response to alternative therapies (e.g., cyproheptadine, dronabinol, megestrol acetate or testosterone if hypogonadal) unless the member has a contraindication or intolerance to alternative therapies
2. Member is currently on antiretroviral therapy
3. Pretreatment BMI is < 18.5 kg/m² (see Appendix C)

J. Short Bowel Syndrome
Authorization of a lifetime total of 8 weeks may be granted to members with short bowel syndrome when GH will be used in conjunction with optimal management of SBS.

V. CONTINUATION OF THERAPY

A. Pediatric GH Deficiency, Turner Syndrome, Noonan Syndrome, CKD, SGA, SHOX deficiency, Congenital Adrenal Hyperplasia, Cerebral Palsy, Cystic Fibrosis, and Russell-Silver Syndrome
Authorization of 12 months may be granted for continuation of therapy when ALL of the following criteria are met:
1. Epiphyses are open (confirmed by X-ray or X-ray is not available)
2. Member’s growth rate is > 2 cm/year unless there is a documented clinical reason for lack of efficacy (e.g., on treatment less than 1 year, nearing final adult height/late stages of puberty)

B. Prader-Willi Syndrome
Authorization of 12 months may be granted for continuation of therapy when the member’s body composition and psychomotor function have improved or stabilized in response to GH therapy.

C. Adult GH Deficiency
Authorization of 12 months may be granted for continuation of therapy when all criteria for initial authorization are met (refer to Section IV. I. above).

D. HIV-Associated Wasting/Cachexia
Authorization of 12 weeks may be granted for continuation of therapy when ALL of the following criteria are met:
1. Member is currently on antiretroviral therapy.
2. Current BMI is < 27 kg/m² (see Appendix C).

VI. APPENDICES
A. Appendix A: Examples of Hypothalamic/Pituitary/CNS Disorders

1. Congenital genetic abnormalities
   a. Known mutations in growth-hormone-releasing hormone (GHRH) receptor, GH gene, GH receptor, or pituitary transcription factors

2. Congenital structural abnormalities
   a. Optic nerve hypoplasia/septo-optic dysplasia
   b. Agenesis of corpus callosum
   c. Empty sella syndrome
   d. Ectopic posterior pituitary
   e. Pituitary aplasia/hypoplasia
   f. Pituitary stalk defect
   g. Anencephaly or prosencephaly
   h. Other mid-line defects
   i. Vascular malformations

3. Acquired structural abnormalities (or causes of hypothalamic/pituitary damage)
   a. CNS tumors/neoplasms (e.g., craniopharyngioma, glioma, pituitary adenoma)
   b. Cysts (Rathke cleft cyst or arachnoid cleft cyst)
   c. Surgery
   d. Radiation
   e. Chemotherapy
   f. CNS infections
   g. CNS infarction (e.g., Sheehan’s syndrome)
   h. Inflammatory lesions (e.g., autoimmune hypophysitis)
   i. Infiltrative lesions (e.g., sarcoidosis, histiocytosis)
   j. Head trauma/traumatic brain injury
   k. Aneurysmal subarachnoid hemorrhage

B. Appendix B: Pituitary Hormones (Other than Growth Hormone)

1. Adrenocorticotropic hormone (ACTH)
2. Antidiuretic hormone (ADH)
3. Follicle stimulating hormone (FSH)
4. Luteinizing hormone (LH)
5. Thyroid stimulating hormone (TSH)
6. Prolactin

C. Appendix C: Calculation of BMI

\[
\text{BMI} = \frac{\text{Weight (pounds)} \times 703}{[\text{Height (inches)}]^2} \quad \text{OR} \quad \frac{\text{Weight (kg)}}{[\text{Height (m)}]^2}
\]

BMI classification:
- Underweight: < 18.5 kg/m²
- Normal weight: 18.5 – 24.9 kg/m²
- Overweight: 25 – 29.9 kg/m²
- Obesity (class 1): 30 – 34.9 kg/m²
- Obesity (class 2): 35 – 39.9 kg/m²
- Extreme obesity: ≥ 40 kg/m²

VII. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

HAEGARDA (C1 Esterase Inhibitor Subcutaneous [Human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Routine prophylaxis to prevent Hereditary Angioedema (HAE) attacks in adolescent and adult patients

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR APPROVAL

Indefinite authorization may be granted for prevention of hereditary angioedema attacks when either of the following criteria is met:

A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing.
B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
   1. Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing, or
   2. Member has a family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

ENHANCED SPECIALTY GUIDELINE MANAGEMENT

HAEGARDA (C1 Esterase Inhibitor Subcutaneous [Human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Routine prophylaxis to prevent Hereditary Angioedema (HAE) attacks in adolescent and adult patients

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review: C4 levels and C1 inhibitor functional and antigenic protein levels.

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for prevention of hereditary angioedema attacks when either of the following criteria is met:
A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing.
B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
   1. Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing, or
   2. Member has a family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy when all of the following criteria are met:
A. Member meets the criteria for initial approval.
B. Member has experienced reduction in frequency, severity and duration of attacks since starting treatment.

V. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

HALAVEN (eribulin mesylate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Halaven is indicated for the treatment of patients with metastatic breast cancer who have previously received at least two chemotherapeutic regimens for the treatment of metastatic disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting.
   2. Halaven is indicated for the treatment of patients with unresectable or metastatic liposarcoma who have received a prior anthracycline-containing regimen.

B. Compendial Uses
   1. Breast cancer
      a. Recurrent or stage IV (M1) human epidermal growth factor receptor 2 (HER2)-negative breast cancer
      b. Recurrent or stage IV (M1) human epidermal growth factor receptor 2 (HER2)-positive breast cancer
   2. Soft tissue sarcoma
      a. Angiosarcoma
      b. Retroperitoneal/intra-abdominal soft tissue sarcoma
      c. Rhabdomyosarcoma
      d. Extremity/superficial trunk, head/neck

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Breast Cancer
   Authorization of 12 months may be granted for treatment of breast cancer.

B. Soft Tissue Sarcoma
   Authorization of 12 months may be granted for treatment of any of the following types of soft tissue sarcoma:
   1. Liposarcoma
   2. Angiosarcoma
   3. Rhabdomyosarcoma
   4. Retroperitoneal/intra-abdominal soft tissue sarcoma
   5. Extremity/superficial trunk, head/neck
III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

HARVONI (ledipasvir and sofosbuvir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Harvoni is indicated for the treatment of:

1. Adult patients with chronic hepatitis C virus (HCV):
   a. genotype 1, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis
   b. genotype 1 infection with decompensated cirrhosis, for use in combination with ribavirin
   c. genotype 1 or 4 infection who are liver transplant recipients without cirrhosis or with compensated cirrhosis, in combination with ribavirin

2. Pediatric patients 12 years of age and older or weighing at least 35 kg with HCV genotype 1, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR APPROVAL

A. Chronic hepatitis C virus infection, without ribavirin

1. Genotype 1 infection
   a. Authorization of up to 12 weeks total may be granted for treatment-naïve members with compensated cirrhosis.
   b. Authorization of up to 12 weeks total may be granted for treatment-naïve members without cirrhosis who have HIV co-infection, are African American, are less than 18 years of age, or have pre-treatment HCV RNA greater than or equal to 6 million IU/mL.
   c. Authorization of up to 8 weeks total may be granted for treatment-naïve members without cirrhosis who have pre-treatment HCV RNA below 6 million IU/mL and are HIV-uninfected and non-African American.
   d. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with peginterferon alfa (PEG-IFN) and ribavirin (RBV) with or without an HCV protease inhibitor (telaprevir, boceprevir, or simeprevir).
   e. Authorization of up to 24 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor.

2. Genotype 4 infection
   Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naïve or who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor.

3. Genotype 5 infection
Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naive or who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor.

4. **Genotype 6 infection**
   Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naive or who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor.

5. **Decompensated cirrhosis (CTP class B or C)**
   Authorization of up to 24 weeks total may be granted for members with HCV genotype 1, 4, 5 or 6 infection and documented anemia (baseline Hgb below 10 g/dL) or RBV ineligibility (see Section IV).

6. **Kidney transplant recipients**
   Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have HCV genotype 1 or 4 infection.

**B. Chronic hepatitis C virus infection, in combination with ribavirin**

1. **Genotype 1 infection**
   a. Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor.
   b. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with sofosbuvir (Sovaldi) plus RBV with or without PEG-IFN.

2. **Genotype 4 infection**
   Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor.

3. **Decompensated cirrhosis (CTP class B or C)**
   a. Authorization of up to 12 weeks total may be granted for members with HCV genotype 1, 4, 5 or 6 infection.
   b. Authorization of up to 24 weeks total may be granted for members with HCV genotype 1, 4, 5 or 6 infection who failed prior treatment with a sofosbuvir-based regimen (eg, sofosbuvir and RBV, sofosbuvir plus PEG-IFN and RBV, sofosbuvir plus simeprevir with or without RBV).
   c. Authorization of up to 12 weeks total may be granted for members with recurrent HCV genotype 1, 4, 5 or 6 infection post liver transplantation and decompensated cirrhosis (see section B.4 below).

4. **Recurrent HCV infection post liver transplantation**
   Authorization of up to 12 weeks total may be granted for members with recurrent HCV genotype 1, 4, 5 or 6 infection post liver transplantation.

**C. HCV and HIV coinfection**
   Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A or B above are met.

**III. CONTINUATION OF THERAPY**

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

**IV. APPENDIX: RIBAVIRIN INELIGIBILITY**
RBV ineligibility is defined as one or more of the below:
- Intolerance to RBV
- Pregnant female or male whose female partner is pregnant
- Hemoglobinopathy
- Coadministration with didanosine
- History of significant or unstable cardiac disease

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

NOVAREL (chorionic gonadotropin)
PREGNYL (chorionic gonadotropin)
OVIDREL (choriogonadotropin alfa)
*Hereafter, hCG will be used to describe all products

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Novarel and Pregnyl are indicated for:
1. Prepubertal cryptorchidism not due to anatomic obstruction
2. Selected cases of hypogonadotropic hypogonadism (hypogonadism secondary to a pituitary deficiency) in males
3. Induction of ovulation and pregnancy in the anovulatory, infertile woman in whom the cause of anovulation is secondary and not due to primary ovarian failure, and who has been appropriately pretreated with human menotropins

Ovidrel is indicated for:
1. Induction of final follicular maturation and early luteinization in infertile women who have undergone pituitary desensitization and who have been appropriately pretreated with follicle stimulating hormones as part of an assisted reproductive technology (ART) program such as in vitro fertilization and embryo transfer
2. Induction of ovulation and pregnancy in anovulatory infertile patients in whom the cause of infertility is functional and not due to primary ovarian failure

B. Compendial Uses

1. Prepubertal cryptorchidism
2. Hypogonadotropic hypogonadism in males
3. Infertility, luteal phase support

All other indications are considered experimental/investigational and are not a covered benefit.

II. MEDICAL BENEFIT ALIGNMENT

Specialty Guideline Management coverage review will be bypassed for drug(s) being requested for a procedure that has been approved under a member’s medical benefit plan. Such members will be exempt from the requirements in Sections IV and V. A medical authorization number and confirmation of the approved procedure(s) will be required.
NOTE: Some plans may opt-out of medical benefit alignment. Members receiving coverage under such plans must meet the requirements in Sections IV and V.

III. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review for hypogonadotropic hypogonadism: testosterone, FSH, and LH levels.

IV. CRITERIA FOR INITIAL APPROVAL

A. Induction of oocyte maturation and/or release
   Authorization of 12 months may be granted for members undergoing ovulation induction or assisted reproductive technology (ART).

B. Prepubertal cryptorchidism
   Authorization of 6 months may be granted for treatment of prepubertal cryptorchidism.

C. Hypogonadotropic hypogonadism
   Authorization of 12 months may be granted for treatment of hypogonadotropic hypogonadism in members who meet both of the following criteria:
   1. Low pretreatment testosterone levels
   2. Low or low-normal follicle stimulating hormone (FSH) or luteinizing hormone (LH) levels

V. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

VI. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT
HEMLIBRA (emicizumab-kxwh)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Hemlibra is indicated for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients ages newborn and older with hemophilia A (congenital factor VIII deficiency) with or without factor VIII inhibitors

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of hemophilia A (congenital factor VIII deficiency).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain reduction in the frequency of bleeding episodes.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

HERCEPTIN HYLECTA (trastuzumab and hyaluronidase-oysk)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Herceptin Hylecta is indicated for adjuvant treatment of adults with HER2 overexpressing node positive or node negative (ER/PR negative or with one high risk feature) breast cancer:
   1. As part of a treatment regimen consisting of doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel
   2. As part of a treatment regimen with docetaxel and carboplatin
   3. As a single agent following multi-modality anthracycline based therapy

B. Herceptin Hylecta is indicated in adults:
   1. In combination with paclitaxel for first-line treatment of HER2-overexpressing metastatic breast cancer
   2. As a single agent for treatment of HER2-overexpressing breast cancer in patients who have received one or more chemotherapy regimens for metastatic disease

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR APPROVAL

Breast Cancer

Authorization of 12 months may be granted for the treatment of adjuvant early stage or metastatic HER2-overexpressing breast cancer.

III. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

HERCEPTIN (trastuzumab)
KANJINTI (trastuzumab-anns)
TRAZIMERA (trastuzumab-qyyyp)
OGIVRI (trastuzumab-dkst)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Adjuvant breast cancer
      Treatment of human epidermal growth factor receptor 2 (HER2)-overexpressing node positive or node negative (estrogen receptor (ER)/progesterone receptor (PR) negative or with one high risk feature) breast cancer:
      a. As part of a treatment regimen consisting of doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel
      b. As part of a treatment regimen with docetaxel and carboplatin
      c. As a single agent following multi-modality anthracycline based therapy
   2. Metastatic breast cancer
      a. In combination with paclitaxel for first-line treatment of HER2-overexpressing metastatic breast cancer
      b. As a single agent for treatment of HER2-overexpressing breast cancer in patients who have received one or more chemotherapy regimens for metastatic disease
   3. Metastatic gastric cancer
      In combination with cisplatin and capecitabine or 5-fluorouracil, for the treatment of patients with HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma, who have not received prior treatment for metastatic disease

B. Compendial Uses
   1. HER2-positive breast cancer
      a. Neoadjuvant therapy
      b. Treatment of recurrent or stage IV (M1) disease
   2. Intra-cerebrospinal fluid (CSF) treatment for leptomeningeal metastases from breast cancer
   3. HER2-positive esophageal and esophagogastric junction cancer
   4. HER2-positive advanced and recurrent uterine serous carcinoma

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Breast Cancer
   1. Authorization of 6 months may be granted for neoadjuvant treatment of HER2-positive breast cancer.
   2. Authorization of up to 12 months total may be granted for adjuvant treatment of HER2-positive breast cancer.
3. Authorization of 12 months may be granted for treatment of HER2-positive recurrent or metastatic breast cancer.
4. Authorization of 12 months may be granted for intra-CSF treatment for leptomeningeal metastases from breast cancer.

B. Esophageal, Gastric, or Gastroesophageal Junction Cancer
Authorization of 12 months may be granted for treatment of HER2-positive esophageal, gastric, or gastroesophageal junction cancer.

C. Uterine Serous Carcinoma
Authorization of 12 months may be granted for treatment of HER2-positive advanced and recurrent uterine serous carcinoma.

III. CONTINUATION OF THERAPY
All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

HETLIOZ (tasimelteon)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Hetlioz is indicated for the treatment of Non-24-Hour Sleep-Wake Disorder (Non-24).

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Non-24-Hour Sleep-Wake Disorder
Authorization of 6 months may be granted for treatment of Non-24-Hour Sleep-Wake Disorder when all of the following criteria are met:
A. The member has a diagnosis of total blindness in both eyes (e.g., nonfunctioning retinas).
B. The member is not able to perceive light in either eye.

III. CONTINUATION OF THERAPY

Non-24-Hour Sleep-Wake Disorder
Authorization of 12 months may be granted for treatment of Non-24-Hour Sleep-Wake Disorder when all of the following criteria are met:
A. The member has a diagnosis of total blindness in both eyes (e.g., nonfunctioning retinas).
B. The member is not able to perceive light in either eye.
C. The member is experiencing increased total nighttime sleep and/or decreased daytime nap duration.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

Subcutaneous Immune Globulin (SCIG):
Hizentra®, HyQvia®, Cutaquig® Cuvitru™ and Xembify®

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
A. Cutaquig (Immune Globulin Subcutaneous [Human] - hipp, 16.5% Solution)
   Cutaquig is indicated as replacement therapy for primary humoral immunodeficiency (PI) in adults.

B. Cuvitru (Immune Globulin Subcutaneous [Human], 20% Solution)
   Cuvitru is indicated as replacement therapy for primary humoral immunodeficiency in adult and pediatric patients two years of age and older.

C. Hizentra (Immune Globulin Subcutaneous [Human], 20% Liquid)
   1. Hizentra is indicated for the treatment of primary immunodeficiency in adults and pediatric patients 2 years of age and older.

   2. Hizentra is indicated for the treatment of adult patients with chronic inflammatory demyelinating polyneuropathy (CIDP) as maintenance therapy to prevent relapse of neuromuscular disability and impairment.

   Limitations of Use:
   Hizentra maintenance therapy in CIDP has been systematically studied for 6 months and for a further 12 months in a follow-up study. Maintenance therapy beyond these periods should be individualized based upon the patient’s response and need for continued therapy.

D. HyQvia (Immune Globulin Infusion 10% [Human] with Recombinant Human Hyaluronidase)
   HyQvia is indicated for the treatment of primary immunodeficiency in adults.

   Limitation of use: Safety and efficacy of chronic use of recombinant human hyaluronidase in HyQvia have not been established in conditions other than primary immunodeficiency.

E. Xembify (Immune Globulin Subcutaneous [Human] – klhw, 20% Solution)
   Xembify is indicated for treatment of primary humoral immunodeficiency (PI) in patients 2 years of age and older.

   All other indications are considered experimental/investigational and are not a covered benefit.
II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review (for primary immunodeficiency only):

A. Diagnostic test results (when applicable)
   1. Copy of laboratory report with serum immunoglobulin levels: IgG, IgA, IgM, and IgG subclasses
   2. Vaccine response to pneumococcal polysaccharide vaccine (post-vaccination *Streptococcus pneumoniae* antibody titers)
   3. Copy of laboratory report with lymphocyte subset enumeration by flow cytometry
   4. Pertinent genetic or molecular testing in members with a known genetic disorder

B. IgG trough level for those continuing with SCIG therapy

III. CRITERIA FOR INITIAL APPROVAL

A. Primary Immunodeficiency

   Initial authorization of 12 months may be granted for members with any of the following diagnoses:

   1. Severe combined immunodeficiency (SCID) or congenital agammaglobulinemia (eg, X-linked or autosomal recessive agammaglobulinemia):
      a. Diagnosis confirmed by genetic or molecular testing, or
      b. Pretreatment IgG level < 200 mg/dL, or
      c. Absence or very low number of T cells (CD3 T cells < 300/microliter) or the presence of maternal T cells in the circulation (SCID only)

   2. Wiskott-Aldrich syndrome, DiGeorge syndrome, or ataxia-telangiectasia (or other non-SCID combined immunodeficiency):
      a. Diagnosis confirmed by genetic or molecular testing (if applicable), and
      b. History of recurrent bacterial infections (eg, pneumonia, otitis media, sinusitis, sepsis, gastrointestinal), and
      c. Impaired antibody response to pneumococcal polysaccharide vaccine (see Appendix)

   3. Common variable immunodeficiency (CVID):
      a. Age 4 years or older
      b. Other causes of immune deficiency have been excluded (eg, drug induced, genetic disorders, infectious diseases such as HIV, malignancy)
      c. Pretreatment IgG level < 500 mg/dL or ≥ 2 SD below the mean for age
      d. History of recurrent bacterial infections
      e. Impaired antibody response to pneumococcal polysaccharide vaccine (see Appendix)

   4. Hypogammaglobulinemia (unspecified), IgG subclass deficiency, selective IgA deficiency, selective IgM deficiency, or specific antibody deficiency:
      a. History of recurrent bacterial infections
      b. Impaired antibody response to pneumococcal polysaccharide vaccine (see Appendix)
      c. Any of the following pre-treatment laboratory findings:
         i. Hypogammaglobulinemia: IgG < 500 mg/dL or ≥ 2 SD below the mean for age
         ii. Selective IgA deficiency: IgA level < 7 mg/dL with normal IgG and IgM levels
         iii. Selective IgM deficiency: IgM level < 30 mg/dL with normal IgG and IgA levels
         iv. IgG subclass deficiency: IgG1, IgG2, or IgG3 ≥ 2 SD below mean for age assessed on at least 2 occasions; normal IgG (total) and IgM levels, normal/low IgA levels
         v. Specific antibody deficiency: normal IgG, IgA and IgM levels

   5. Other predominant antibody deficiency disorders must meet a., b., and c.i. in section 4. above.

   6. Other combined immunodeficiency must meet criteria in section 2. above.
B. Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) (Hizentra only)
Initial authorization of 3 months may be granted for the maintenance treatment of CIDP in members currently receiving intravenous immune globulin (IVIG) therapy.

IV. CONTINUATION OF THERAPY
The following criteria apply to members who are currently receiving SCIG therapy through a paid pharmacy or medical benefit. All other members (including new members) must meet initial authorization criteria.

A. Primary Immunodeficiency
Authorization of 24 months may be granted when the following criteria are met:
1. A reduction in the frequency of bacterial infections has been demonstrated since initiation of SCIG therapy, AND
2. IgG trough levels are monitored at least yearly and maintained at or above the lower range of normal for age (when applicable for indication), OR
3. The prescriber will re-evaluate the dose of SCIG and consider a dose adjustment (when appropriate).

B. Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) (Hizentra only)
Authorization of 24 months may be granted when the following criteria are met
1. Maintenance of response from previous IVIG therapy
2. SCIG is being used at the lowest effective dose

V. APPENDIX
Impaired Antibody Response to Pneumococcal Polysaccharide Vaccine:
- Age 2 years and older: impaired antibody response demonstrated to vaccination with a pneumococcal polysaccharide vaccine
- Not established for children less than 2 years of age
- Excludes the therapy initiated in the hospital setting

VI. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

HUMIRA (adalimumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Moderately to severely active rheumatoid arthritis (RA)
   2. Moderately to severely active polyarticular juvenile idiopathic arthritis (pJIA)
   3. Active psoriatic arthritis (PsA)
   4. Active ankylosing spondylitis (AS)
   5. Moderately to severely active Crohn’s disease (CD)
   6. Moderate to severely active ulcerative colitis (UC)
   7. Moderate to severe chronic plaque psoriasis (PsO)
   8. Moderate to severe hidradenitis suppurativa
   9. Non-infectious intermediate, posterior and panuveitis

B. Compendial Uses
   Axial spondyloarthritis

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active rheumatoid arthritis (RA)
   1. Authorization of 24 months may be granted for members who have previously received Humira or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) indicated for moderately to severely active rheumatoid arthritis.

   2. Authorization of 24 months may be granted for treatment of moderately to severely active RA when any of the following criteria is met:
      a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
      b. Member has an intolerance or contraindication to methotrexate (see Appendix A).

B. Moderately to severely active polyarticular juvenile idiopathic arthritis (pJIA)
   1. Authorization of 24 months may be granted for members who have previously received Humira or any other biologic DMARD indicated for moderately to severely active polyarticular juvenile idiopathic arthritis.

   2. Authorization of 24 months may be granted for treatment of active pJIA when any of the following criteria is met:
      a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate.
b. Member has intolerance or contraindication to methotrexate (see Appendix A).

C. **Active psoriatic arthritis (PsA)**
   Authorization of 24 months may be granted for treatment of active psoriatic arthritis (PsA).

D. **Active ankylosing spondylitis (AS) and axial spondyloarthritis**
   1. Authorization of 24 months may be granted for members who have previously received Humira or any other biologic DMARD indicated for active ankylosing spondylitis.
   2. Authorization of 24 months may be granted for treatment of active ankylosing spondylitis and axial spondyloarthritis when any of the following criteria is met:
      a. Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs).
      b. Member has an intolerance or contraindication to two or more NSAIDs.

E. **Moderately to severely active Crohn's disease (CD)**
   1. Authorization of 24 months may be granted for members who have previously received Humira or any other biologic indicated for the treatment of Crohn’s disease.
   2. Authorization of 24 months may be granted for treatment of moderately to severely active CD when the member has had an inadequate response, intolerance or contraindication to at least one conventional therapy option (see Appendix B).

F. **Moderately to severely active ulcerative colitis (UC)**
   1. Authorization of 24 months may be granted for members who have previously received Humira or any other biologic or targeted synthetic disease modifying drug (e.g., Xeljanz) indicated for moderately to severely active ulcerative colitis.
   2. Authorization of 24 months may be granted for treatment of moderately to severely active UC when the member has had an inadequate response, intolerance or contraindication to at least one conventional therapy option (see Appendix C).

G. **Moderate to severe chronic plaque psoriasis (PsO)**
   1. Authorization of 24 months may be granted for members who have previously received Humira, Otezla, or any other biologic DMARD indicated for the treatment of moderate to severe chronic plaque psoriasis.
   2. Authorization of 24 months may be granted for treatment of moderate to severe chronic plaque psoriasis when all of the following criteria are met:
      a. At least 5% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
      b. Member meets any of the following criteria:
         i. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or a pharmacologic treatment with methotrexate, cyclosporine or acitretin.
         ii. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine or acitretin (see Appendix D).
         iii. Member has severe psoriasis that warrants a biologic DMARD as first-line therapy.

H. **Moderate to severe hidradenitis suppurativa**
   Authorization of 24 months may be granted for treatment of moderate to severe hidradenitis suppurativa.
I. Uveitis (non-infectious intermediate, posterior and panuveitis)
   Authorization of 24 months may be granted for treatment of non-infectious intermediate, posterior and panuveitis.

III. CONTINUATION OF THERAPY

   A. For ulcerative colitis:
      Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve clinical remission by treatment day 56 (week 8) and maintain positive clinical response with Humira thereafter as evidenced by low disease activity or improvement in signs and symptoms of ulcerative colitis.

   B. For all other indications:
      Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Humira as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

   For all indications: Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB)

   Note: Members who have received Humira or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) are exempt from requirements related to TB screening in this Policy.

V. APPENDICES

   Appendix A: Examples of Contraindications to Methotrexate
   1. Alcoholism, alcoholic liver disease or other chronic liver disease
   2. Breastfeeding
   3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
   4. Elevated liver transaminases
   5. History of intolerance or adverse event
   6. Hypersensitivity
   7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
   8. Myelodyplasia
   9. Pregnancy or planning pregnancy
   10. Renal impairment
   11. Significant drug interaction

   Appendix B: Examples of Conventional Therapy Options for CD
   1. Mild to moderate disease – induction of remission:
      a. Oral budesonide
      b. Alternatives: metronidazole, ciprofloxacin, rifaximin
   2. Mild to moderate disease – maintenance of remission:
      a. Azathioprine, mercaptopurine
      b. Alternatives: oral budesonide, methotrexate intramuscularly (IM) or subcutaneously (SC), sulfasalazine
   3. Moderate to severe disease – induction of remission:
      a. Prednisone, methylprednisolone intravenously (IV)
b. Alternatives: methotrexate IM or SC

4. Moderate to severe disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: methotrexate IM or SC

5. Perianal and fistulizing disease – induction of remission
   a. Metronidazole ± ciprofloxacin, tacrolimus

6. Perianal and fistulizing disease – maintenance of remission
   a. Azathioprine, mercaptopurine
   b. Alternative: methotrexate IM or SC

Appendix C: Examples of Conventional Therapy Options for UC

1. Mild to moderate disease – induction of remission:
   a. Oral mesalamine (e.g., Asacol, Asacol HD, Lialda, Pentasa), balsalazide, olsalazine
   b. Rectal mesalamine (e.g., Canasa, Rowasa)
   c. Rectal hydrocortisone (e.g., Colocort, Cortifoam)
   d. Alternatives: prednisone, azathioprine, mercaptopurine, sulfasalazine

2. Mild to moderate disease – maintenance of remission:
   a. Oral mesalamine, balsalazide, olsalazine, rectal mesalamine
   b. Alternatives: azathioprine, mercaptopurine, sulfasalazine

3. Severe disease – induction of remission:
   a. Prednisone, hydrocortisone IV, methylprednisolone IV
   b. Alternatives: cyclosporine IV, tacrolimus, sulfasalazine

4. Severe disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: sulfasalazine

5. Pouchitis: Metronidazole, ciprofloxacin
   a. Alternative: rectal mesalamine

Appendix D: Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin.

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Drug interaction
4. Cannot be used due to risk of treatment-related toxicity
5. Pregnancy or planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VI. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

DUROLANE (hyaluronic acid)
EUFLEXXA (1% sodium hyaluronate)
GEL-ONE (cross-linked hyaluronate)
GELSYN-3 (sodium hyaluronate 0.84%)
GENVISC 850 (sodium hyaluronate)
HYALGAN (sodium hyaluronate)
HYMOVIS (high molecular weight viscoelastic hyaluronan)
MONOVISC (high molecular weight hyaluronan)
ORTHOVISC (high molecular weight hyaluronan)
SUPARTZ (sodium hyaluronate)
SYNVISC (hylan G-F 20)
SYNVISC ONE (hylan G-F 20)
TRIVISC (sodium hyaluronate)
VISCO-3 (sodium hyaluronate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
   Treatment of pain in osteoarthritis of the knee in patients who have failed to respond adequately to conservative non-pharmacologic therapy and simple analgesics (e.g., acetaminophen)

B. Compendial Uses
   1. Treatment of pain in osteoarthritis of the shoulder
   2. Treatment of pain in osteoarthritis of the hip

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Osteoarthritis (OA) of the Knee, Hip, or Shoulder
Authorization of 12 months may be granted for treatment of osteoarthritis (OA) in the knee, hip or shoulder.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.
IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

HYCAMTIN CAPSULES (topotecan)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Hycamtin capsules are indicated for the treatment of relapsed small cell lung cancer (SCLC) in patients with a prior complete or partial response and who are at least 45 days from the end of first-line chemotherapy.

B. Compendial Uses

1. SCLC
2. Merkel Cell Carcinoma, disseminated, distant metastatic (clinical M1), if contraindications to checkpoint immunotherapy

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Small cell lung cancer (SCLC)

Authorization of 12 months may be granted for treatment of small cell lung cancer.

B. Merkel Cell Carcinoma

Authorization of 12 months may be granted for treatment of Merkel cell carcinoma when all of the following criteria are met:

1. Member has disseminated distant metastatic disease.
2. Member has contraindications to checkpoint immunotherapy [e.g., Bavencio (avelumab), Keytruda (pembrolizumab)].

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

MAKENA (hydroxyprogesterone caproate)
hydroxyprogesterone caproate (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Makena is indicated to reduce the risk of preterm birth in women with a singleton pregnancy who have a history of singleton spontaneous preterm birth. The effectiveness of Makena is based on improvement in the proportion of women who delivered < 37 weeks of gestation. There are no controlled trials demonstrating a direct clinical benefit, such as improvement in neonatal mortality and morbidity.

Limitation of use: While there are many risk factors for preterm birth, safety and efficacy of Makena has been demonstrated only in women with a prior spontaneous singleton preterm birth. It is not intended for use in women with multiple gestations or other risk factors for preterm birth.

All other indications are considered experimental/investigational and are not a covered benefit.

II. EXCLUSIONS

Coverage will not be provided for members with any of the following exclusions:
A. Current or history of thrombosis or thromboembolic disorders
B. Known or suspected breast cancer, other hormone-sensitive cancer, or a history of these conditions
C. Undiagnosed abnormal vaginal bleeding unrelated to pregnancy
D. Cholestatic jaundice of pregnancy
E. Liver tumors, benign or malignant, or active liver disease
F. Uncontrolled hypertension

III. CRITERIA FOR INITIAL APPROVAL

Prevention of preterm birth
Authorization of 21 weeks or through 36 weeks, 6 days of gestational age, whichever is less, may be granted for the prevention of preterm birth when all of the following criteria are met:
A. The current pregnancy is a singleton pregnancy.
B. The member has a history of singleton spontaneous preterm birth, defined as delivery at less than 37 weeks gestation following preterm labor, preterm rupture of membranes, and cervical insufficiency.
C. Makena will be initiated between 16 weeks, 0 days and 24 weeks, 6 days of gestation.
IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

IBRANCE (palbociclib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Ibrance is indicated for the treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with:

1. an aromatase inhibitor as initial endocrine based therapy in postmenopausal women or in men, or
2. fulvestrant in women with disease progression following endocrine therapy.

B. Compendial Uses

Soft tissue sarcoma: well-differentiated/dedifferentiated liposarcoma

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Breast cancer

Authorization of 12 months may be granted for the treatment of HR-positive HER2-negative breast cancer when one of the following criteria is met:

1. Ibrance is used in combination with an aromatase inhibitor (e.g., anastrozole, exemestane, letrozole).
2. Ibrance is used in combination with fulvestrant.

B. Soft tissue sarcoma

Authorization of 12 months may be granted for treatment of well-differentiated/dedifferentiated liposarcoma.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

ENHANCED SPECIALTY GUIDELINE MANAGEMENT

FIRAZYR (icatibant)
icatibant (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Treatment of acute attacks of hereditary angioedema in adults 18 years of age and older

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. C4 levels and C1 inhibitor functional and antigenic protein levels
B. F12, angiopoietin-1 or plasminogen gene mutation testing, if applicable
C. Chart notes confirming family history of angioedema, if applicable

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of acute hereditary angioedema attacks when the requested medication will not be used in combination with Berinert, Kalbitor, or Ruconest, and either of the following criteria is met:
A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing:
   1. C1 inhibitor (C1-INH) antigenic level is below the lower limit of normal as defined by the laboratory performing the test, or
   2. Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test).
B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
   1. Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing, or
   2. Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy when all of the following criteria are met:
A. Member meets the criteria for initial approval.
B. Member has experienced reduction in severity and/or duration of attacks when they use the requested medication to treat an acute attack.

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

ICLUSIG (ponatinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Adult patients with chronic phase, accelerated phase, or blast phase chronic myeloid leukemia (CML) or Ph+ ALL for whom no other tyrosine kinase inhibitor (TKI) therapy is indicated
   2. Adult patients with T315I-positive CML (chronic phase, accelerated phase, or blast phase) or T315I-positive Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL)

   Limitation of use: Iclusig is not indicated and is not recommended for the treatment of patients with newly diagnosed chronic phase CML.

B. Compendial Uses
   1. Primary treatment of advanced phase CML (accelerated phase or blast phase)
   2. Follow-up therapy for after hematopoietic stem cell transplant (HSCT) for CML and ALL patients
   3. Treatment of Ph+ ALL

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review:

A. Prior to initiation of therapy for treatment of CML or Ph+ ALL: results of cytogenetic and/or molecular testing for detection of the Ph chromosome or the BCR-ABL gene

B. For members requesting initiation of Iclusig therapy for treatment of T315I-positive CML: results of T315I mutation testing

III. CRITERIA FOR INITIAL APPROVAL

A. Chronic Myeloid Leukemia (CML)

Authorization of 6 months may be granted for treatment of CML that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when any of the following criteria are met:

   1. Member has T315I-positive CML OR treatment with any other TKI is not indicated for the member (e.g., bosutinib, dasatinib, imatinib, nilotinib)
   2. Member has accelerated phase (AP) or blast phase (BP) disease
   3. Member has received HSCT for CML
B. Ph+ Acute Lymphoblastic Leukemia (ALL)/Lymphoblastic Lymphoma (LL)
Authorization of 12 months may be granted for treatment of Ph+ ALL or LL that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when the member has T315I-positive disease OR treatment with any other TKI is not indicated for the member (e.g., bosutinib, dasatinib, imatinib, nilotinib).

IV. CONTINUATION OF THERAPY

A. CML
Authorization of 12 months may be granted for continued treatment of CML that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when any of the following criteria are met:
1. BCR-ABL1 ≤ 10% for members who have been receiving Iclusig for ≤ 12 months
2. No evidence of disease progression for members who have been receiving Iclusig for > 12 months
3. Member has received HSCT

B. Ph+ ALL/LL
Authorization of 12 months may be granted for continued treatment of Ph+ ALL or LL that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when either of the following criteria are met:
1. Member has not experienced disease progression or an unacceptable toxicity
2. Member has received HSCT

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

IDHIFA (enasidenib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Idhifa is indicated for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with an isocitrate dehydrogenase-2 (IDH-2) mutation as detected by an FDA-approved test.

B. Compendial Uses

1. Induction therapy for patients 60 years of age or greater with isocitrate dehydrogenase-2 (IDH-2) mutated acute myeloid leukemia (AML) when not a candidate for intensive remission induction therapy or declines intensive therapy.

2. Post-remission therapy for patients greater than 60 years of age with isocitrate dehydrogenase-2 (IDH-2) mutated acute myeloid leukemia (AML) following response to previous lower intensity therapy.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for the treatment of acute myeloid leukemia with an isocitrate dehydrogenase-2 (IDH2) mutation as detected by an FDA-approved test.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

ILARIS (canakinumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Periodic Fever Syndromes:
      - Cryopyrin-Associated Periodic Syndromes (CAPS)
        Ilaris is indicated for the treatment of Cryopyrin-Associated Periodic Syndromes (CAPS), in adults and children 4 years of age and older including Familial Cold Autoinflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS).
      - Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS)
        Ilaris is indicated for the treatment of TRAPS in adult and pediatric patients.
      - Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD)
        Ilaris is indicated for the treatment of HIDS and MKD in adult and pediatric patients.
      - Familial Mediterranean Fever (FMF)
        Ilaris is indicated for the treatment of FMF in adult and pediatric patients.
   2. Active Systemic Juvenile Idiopathic Arthritis (SJIA)
      Ilaris is indicated for the treatment of active Systemic Juvenile Idiopathic Arthritis (SJIA) in patients aged 2 years and older.

B. Compendial Uses
   Treatment of acute gout attacks

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Periodic Fever Syndromes
   Authorization of 24 months may be granted for members who have a diagnosis of ANY of the following:
   1. CAPS, including FCAS and MWS
   2. TRAPS
   3. HIDS or MKD
   4. FMF

B. Active Systemic Juvenile Idiopathic Arthritis (sJIA)
   1. Authorization of 24 months may be granted for the treatment of active sJIA for members who have received Actemra or Kineret in a paid claim through a pharmacy or medical benefit within the previous 120 days.
2. Authorization of 24 months may be granted for the treatment of active sJIA for members who have had an inadequate response to a trial of nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, methotrexate, or leflunomide.

C. Treatment of acute gout attacks
Authorization of 6 months may be granted for members who meet all of the following criteria:
1. Member had two or more gout flares within the previous 12 months
2. Member has had an inadequate response, intolerance, or contraindication to at least two of the following: maximum tolerated dose of an NSAID, colchicine, intra-articular injection of triamcinolone acetonide at doses 40 mg or greater, systemic corticosteroids
3. Member will receive Ilaris concurrently with urate-lowering therapy (i.e., allopurinol, febuxostat)

III. CONTINUATION OF THERAPY

A. Periodic Fever Syndromes
Members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria.

B. Active Systemic Juvenile Idiopathic Arthritis
Authorization of 24 months may be granted for members who have achieved or maintained positive clinical response after at least 3 months of therapy with Ilaris as evidenced by low disease activity or improvement in signs and symptoms.

C. Treatment of acute gout attacks
Authorization of 24 months may be granted for members who have experienced a positive clinical response from treatment with Ilaris (e.g., reduction in swelling within 72 hours, reduction in pain compared to prior attacks, or delayed time to flare compared to prior attacks).

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

ILUMYA (tildrakizumab-asmn)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Treatment of adult patients with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Moderate to severe plaque psoriasis
A. Authorization of 24 months may be granted for members who are 18 years of age or older who have previously received Ilumya, Otezla, or any other biologic DMARD indicated for the treatment of moderate to severe plaque psoriasis.

B. Authorization of 24 months may be granted for treatment of moderate to severe plaque psoriasis for members who are 18 years of age or older when all of the following criteria are met:
   1. At least 5% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
   2. Member meets any of the following criteria:
      i. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
      ii. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine or acitretin (see Appendix).
      iii. Member has severe psoriasis that warrants a biologic DMARD as first-line therapy.

III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 4 months of therapy with Ilumya as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB).

Note: Members who have received Ilumya or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) are exempt from requirements related to TB screening in this Policy.
V. APPENDIX

Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin
1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Cannot be used due to risk of treatment-related toxicity
4. Drug interaction
5. Pregnancy or planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VI. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

GLEEVEC (imatinib mesylate)
imatinib mesylate (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Newly diagnosed adult and pediatric patients with Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase
   2. Patients with Ph+ CML in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy
   3. Adult patients with relapsed or refractory Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL)
   4. Pediatric patients with newly diagnosed Ph+ ALL in combination with chemotherapy
   5. Adult patients with myelodysplastic/myeloproliferative diseases (MDS/MPD) associated with PDGFR (platelet-derived growth factor receptor) gene re-arrangements as determined with an FDA-approved test
   6. Adult patients with aggressive systemic mastocytosis without the D816V c-Kit mutation as determined with an FDA-approved test or with c-Kit mutational status unknown
   7. Adult patients with hypereosinophilic syndrome (HES) and/or chronic eosinophilic leukemia (CEL) who have the FIP1L1-PDGFRα fusion kinase (mutational analysis or FISH demonstration of CHIC2 allele deletion) and for patients with HES and/or CEL who are FIP1L1-PDGFRα fusion kinase negative or unknown
   8. Adult patients with unresectable, recurrent and/or metastatic dermatofibrosarcoma protuberans (DFSP)
   9. Patients with Kit (CD117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumors (GIST)
   10. Adjuvant treatment of adult patients following complete gross resection of Kit (CD117) positive GIST

B. Compendial Uses
   1. Primary treatment of advanced phase CML (accelerated phase or blast phase)
   2. Follow-up therapy for CML patients after hematopoietic stem cell transplant (HSCT)
   3. Induction/consolidation and maintenance therapy for Ph+ ALL
   4. GIST (primary, postoperative and continued treatment)
   5. Desmoid tumors
   6. Pigmented villonodular synovitis/tenosynovial giant cell tumor
   7. Recurrent chordoma
   8. Metastatic or unresectable C-Kit mutated melanoma as second-line or subsequent therapy
   9. AIDS-related Kaposi sarcoma that has progressed on or not responded to first-line systemic therapy
   10. Chronic myelomonocytic leukemia

All other indications are considered experimental/investigational and are not a covered benefit.
II. REQUIRED DOCUMENTATION
The following information is necessary to initiate the prior authorization review prior to initiation of therapy for treatment of CML or Ph+ ALL: results of cytogenetic and/or molecular testing for detection of the Ph chromosome or the BCR-ABL gene.

III. CRITERIA FOR INITIAL APPROVAL

A. Chronic Myeloid Leukemia (CML)
Authorization of 6 months may be granted for treatment of CML that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when the member did not fail (other than due to intolerance) prior therapy with a TKI (e.g., dasatinib, nilotinib, bosutinib, ponatinib).

B. Ph+ Acute Lymphoblastic Leukemia (ALL)/Lymphoblastic Lymphoma (LL)
Authorization of 12 months may be granted for treatment of Ph+ ALL or lymphoblastic lymphoma that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing.

C. Gastrointestinal Stromal Tumor (GIST), Desmoid Tumors, Pigmented Villonodular Synovitis/Tenosynovial Giant Cell Tumor (PVNS/TGCT), Hypereosinophilic Syndrome/Chronic Eosinophilic Leukemia (HES/CEL), Dermatofibrosarcoma Protuberans (DFSP), Chordoma
Authorization of 12 months may be granted for treatment of GIST, desmoid tumors, PVNS/TGCT, HES/CEL, DFSP, or recurrent chordoma

D. Myelodysplastic Syndromes/Myeloproliferative Diseases (MDS/MPD) and Chronic Myelomonocytic Leukemia (CMML)
Authorization of 12 months may be granted for treatment of MDS/MPD or CMML when the member's disease is associated with PDGFR gene rearrangements

E. Aggressive Systemic Mastocytosis (ASM)
Authorization of 12 months may be granted for treatment of ASM without the D816V c-Kit mutation or with c-Kit mutational status unknown.

F. Melanoma
Authorization of 12 months may be granted for treatment of metastatic or unresectable c-Kit mutation-positive melanoma as second-line or subsequent therapy.

G. AIDS-related Kaposi Sarcoma
Authorization of 12 months may be granted for treatment of AIDS-related Kaposi sarcoma that has progressed on or not responded to first-line systemic therapy.

IV. CONTINUATION OF THERAPY

A. CML
Authorization of 12 months may be granted for continued treatment of CML that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when any of the following criteria are met:
1. BCR-ABL1 ≤ 10% for members who have been receiving imatinib/Gleevec for ≤ 12 months
2. No evidence of disease progression for members who have been receiving imatinib/Gleevec for > 12 months
3. Member has received HSCT

B. Ph+ ALL/LL
Authorization of 12 months may be granted for continued treatment of Ph+ ALL or LL that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing in members who have not experienced disease progression or an unacceptable toxicity.

C. GIST, Desmoid Tumors, PVNS/TGCT, HES/CEL, DFSP, Chordoma, MDS/MPD, CMML, ASM, Melanoma, AIDS-related Kaposi sarcoma
Authorization of 12 months may be granted for continued treatment of GIST, desmoid tumors, PVNS/TGCT, HES/CEL, DFSP, recurrent chordoma, MDS/MPD, CMML, ASM, metastatic or unresectable melanoma, or AIDS-related Kaposi sarcoma in members who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

IMBRUVICA (ibrutinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Mantle Cell Lymphoma (MCL)
   Imbruvica is indicated for the treatment of adult patients with MCL who have received at least one prior therapy.

2. Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL)
   i. Imbruvica is indicated for the treatment of adult patients with CLL/SLL.
   ii. Imbruvica is indicated for the treatment of adult patients with CLL/SLL with 17p deletion.

3. Waldenström’s Macroglobulinemia (WM)
   Imbruvica is indicated for the treatment of adult patients with WM.

4. Marginal Zone Lymphoma (MZL)
   Imbruvica is indicated for the treatment of adult patients with MZL who require systemic therapy and have received at least one prior anti-CD20-based therapy.

5. Chronic Graft versus Host Disease (cGVHD)
   Imbruvica is indicated for the treatment of adult patients with cGVHD after failure of one or more lines of systemic therapy.

B. Compendial Use

1. Mantle cell lymphoma, in combination with rituximab as pretreatment in order to limit the number of cycles of less aggressive induction therapy with RHyperCVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone) regimen

2. Gastric MALT lymphoma, second-line or subsequent therapy for recurrent or progressive disease

3. Non-gastric MALT lymphoma, second-line or subsequent therapy for refractory or progressive disease

4. Hairy cell leukemia, for progression

5. Lymphoplasmacytic lymphoma (LPL)

6. Primary central nervous system lymphoma, for relapsed or refractory disease

7. Follicular lymphoma

8. Nodal marginal zone lymphoma, second-line or subsequent therapy for refractory or progressive disease

9. Splenic marginal zone lymphoma, second-line or subsequent therapy for refractory or progressive disease

10. Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma in patients who have received prior chemoimmunotherapy
11. Diffuse large B-cell lymphoma, second-line or subsequent therapy for refractory or progressive disease
12. AIDS-related B-cell lymphoma, for second-line or subsequent therapy for relapsed disease
13. Post-transplant lymphoproliferative disorders, subsequent therapy for patients with partial response, persistent, or progressive disease after receiving chemoimmunotherapy

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Mantle Cell Lymphoma (MCL)
Authorization of 12 months may be granted to members with MCL who meet one of the following criteria:
1. The patient has received at least one prior therapy.
2. Imbruvica will be used in combination with rituximab as pretreatment to induction therapy with RHyperCVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone) regimen.

B. Chronic Lymphocytic Leukemia (CLL) and Small Lymphocytic Lymphoma (SLL)
Authorization of 12 months may be granted to members with CLL/SLL.

C. Waldenström’s Macroglobulinemia/lymphoplasmacytic lymphoma (WM/LPL)
Authorization of 12 months may be granted to members with WM/LPL.

D. Marginal Zone Lymphoma (MZL)
Authorization of 12 months may be granted to members with MZL who require systemic therapy and who have received at least one prior anti-CD20-based therapy.

E. Chronic Graft-Versus-Host Disease (cGVHD)
Authorization of 12 months may be granted to members with cGVHD who have failed one or more lines of systemic therapy.

F. Gastric MALT Lymphoma and Non-gastric MALT Lymphoma
Authorization of 12 months may be granted to members with recurrent, refractory, or progressive gastric or non-gastric MALT lymphoma as second-line or subsequent therapy.

G. Hairy Cell Leukemia
Authorization of 12 months may be granted to members with hairy cell leukemia when Imbruvica is used for disease progression.

H. Primary central nervous system lymphoma
Authorization of 12 months may be granted to members with relapsed or refractory primary central nervous system lymphoma.

I. Follicular lymphoma
Authorization of 12 months may be granted to members with follicular lymphoma.

J. Nodal marginal zone lymphoma
Authorization of 12 months may be granted to members with refractory or progressive nodal marginal zone lymphoma when Imbruvica is used as second-line or subsequent therapy.

K. Splenic marginal zone lymphoma
Authorization of 12 months may be granted to members with refractory or progressive splenic marginal zone lymphoma when Imbruvica is used as second-line or subsequent therapy.

L. Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma
   Authorization of 12 months may be granted to members with histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma in patients who have received prior chemoimmunotherapy.

M. Diffuse large B-cell lymphoma
   Authorization of 12 months may be granted to members with refractory or progressive diffuse large B-cell lymphoma when Imbruvica is used as second-line or subsequent therapy.

N. AIDS-related B-cell lymphoma
   Authorization for 12 months may be granted to members with relapsed AIDS-related B-cell lymphoma when Imbruvica is used as second-line or subsequent therapy.

O. Post-transplant lymphoproliferative disorders
   Authorization for 12 months may be granted to members with partial response, persistent, progressive post-transplant lymphoproliferative disorders after receiving chemoimmunotherapy.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

IMFINZI (durvalumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
A. Locally advanced or metastatic urothelial carcinoma in patients with disease progression during or following platinum-containing chemotherapy or with disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.
B. Unresectable, stage III non-small cell lung cancer (NSCLC) whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Urothelial carcinoma
Authorization of 12 months may be granted for treatment of locally advanced or metastatic urothelial carcinoma when any of the following criteria is met:
   1. Member experienced disease progression during or following platinum-containing chemotherapy.
   2. Member experienced disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

B. Non-small cell lung cancer
Authorization of up to 12 months may be granted for treatment of unresectable, Stage III NSCLC following concurrent platinum-based chemotherapy and radiation therapy.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

IMLYGIC (talimogene laherparepvec)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Imlygic is indicated for the local treatment of unresectable cutaneous, subcutaneous, and nodal lesions in patients with melanoma recurrent after initial surgery.

Limitations of use: Imlygic has not been shown to improve overall survival or have an effect on visceral metastases.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Melanoma
Authorization of 12 months may be granted for treatment of unresectable cutaneous, subcutaneous, and nodal lesions in members with melanoma.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

INBRIJA (levodopa inhalation powder)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Inbrija is indicated for the treatment of OFF episodes in patients with Parkinson’s disease treated with carbidopa/levodopa.

All other indications are considered experimental/investigational and are not a covered benefit.

II. EXCLUSIONS

Coverage will not be provided for members with any of the following exclusions:

A. Asthma
B. Chronic obstructive pulmonary disease (COPD)
C. Other chronic underlying lung disease

III. CRITERIA FOR INITIAL APPROVAL

Parkinson’s disease

Authorization of 6 months may be granted for treatment of Parkinson’s disease when all of the following criteria are met:

A. The patient experiences at least 2 hours per day of off time
B. The patient is currently being treated with oral carbidopa/levodopa
C. Attempts to manage off episodes by adjusting the dosing or formulation of carbidopa/levodopa were ineffective
D. Adjuvant treatment with one of the following therapies was ineffective at managing off episodes:
   1. Dopamine agonist (e.g., pramipexole, ropinirole)
   2. Monoamine oxidase B (MAO-B) inhibitor (e.g., selegiline, rasagiline)
   3. Catechol-O-methyl transferase (COMT) inhibitor (e.g., entacapone, tolcapone)

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for treatment of Parkinson’s disease when all of the following criteria are met:

A. The patient is currently being treated with oral carbidopa/levodopa and at least one of the following:
   1. Dopamine agonist
   2. MAO-B inhibitor
   3. COMT inhibitor
B. The patient is experiencing improvement on Inbrija therapy (e.g., reduction in daily off time, improvement in motor function post-administration)

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

INCRELEX (mecasermin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no contraindications or exclusions to the prescribed therapy.

FDA-Approved Indications

Increlex is indicated for the treatment of growth failure in children with severe primary insulin-like growth factor-1 (IGF-1) deficiency or with growth hormone (GH) gene deletion who have developed neutralizing antibodies to GH.

Severe primary IGF-1 deficiency is defined by:

- Height standard deviation (SD) score ≤ –3.0 and
- Basal IGF-1 SD score ≤ –3.0 and
- Normal or elevated GH.

Severe primary IGF-1 deficiency includes classical and other forms of GH insensitivity. Patients with primary IGF-1 deficiency may have mutations in the GH receptor (GHR), post-GHR signaling pathway including the IGF-1 gene. They are not GH deficient, and therefore, they cannot be expected to respond adequately to exogenous GH treatment. Increlex is not intended for use in subjects with secondary forms of IGF-1 deficiency, such as GH deficiency, malnutrition, hypothyroidism, or chronic treatment with pharmacologic doses of anti-inflammatory steroids. Thyroid and nutritional deficiencies should be corrected before initiating Increlex treatment.

Limitations of use: Increlex is not a substitute to GH for approved GH indications.

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review for continuation of therapy requests:

A. Total duration of treatment (approximate duration is acceptable)
B. Date of last dose administered
C. Approving health plan/pharmacy benefit manager
D. Date of prior authorization/approval
E. Prior authorization approval letter

III. CRITERIA FOR INITIAL APPROVAL

Severe Primary IGF-1 Deficiency
Authorization of 12 months may be granted to members with severe primary IGF-1 deficiency or GH gene deletion with neutralizing antibodies to GH when ALL of the following criteria are met:
A. Pretreatment height is ≥ 3 standard deviations (SD) below the mean for age and gender
B. Pretreatment basal IGF-1 level is ≥ 3 SD below the mean for age and gender
C. Pediatric GH deficiency has been ruled out with a provocative GH test (i.e., peak GH level ≥ 10 ng/mL)
D. Epiphyses are open

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for the continuation of therapy of severe primary IGF-1 deficiency or GH gene deletion with neutralizing antibodies to GH when ALL of the following criteria are met:
A. The member’s growth rate is > 2 cm/year or there is a documented clinical reason for lack of efficacy (e.g., on treatment less than 1 year, nearing final adult height/late stages of puberty).
B. Epiphyses are open (confirmed by X-ray or X-ray is not available).

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

INGREZZA (valbenazine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Treatment of adults with tardive dyskinesia

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR APPROVAL

Tardive dyskinesia
Authorization of 3 months may be granted for members requesting Ingrezza for the treatment of tardive dyskinesia related to drug use.

III. CONTINUATION OF THERAPY

Coverage may be renewed for 12 months in situations where there has been an improvement in signs and symptoms of tardive dyskinesia.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

INLYTA (axitinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
   Inlyta is indicated for the treatment of advanced renal cell carcinoma (RCC) after failure of one prior systemic therapy.

B. Compendial Uses
   1. Relapsed or surgically unresectable stage IV renal cell carcinoma
   2. Papillary, Hürthle cell, or follicular thyroid carcinoma

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Renal Cell Carcinoma
   Authorization of 12 months may be granted for treatment of relapsed, metastatic, or unresectable renal cell carcinoma as a single agent or in combination with pembrolizumab.

B. Papillary, Hürthle cell, or Follicular Thyroid Carcinoma
   Authorization of 12 months may be granted for treatment of radioiodine refractory papillary, Hürthle cell, or follicular thyroid carcinoma.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in Section II when there is no evidence of unacceptable toxicity or disease progression on the current regimen.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

INREBIC (fedratinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Inrebic is indicated for the treatment of adult patients with intermediate-2 or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis (MF).

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Myelofibrosis
Authorization of 12 months may be granted for the treatment of intermediate-2 or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis (MF).

III. CONTINUATION OF THERAPY

Myelofibrosis
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have improvement in symptoms and no unacceptable toxicity.

IV. REFERENCES

Prior Authorization Criteria

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Insomnia Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brand Name*</td>
<td>Belsomra</td>
</tr>
<tr>
<td>(generic)</td>
<td>(suvorexant)</td>
</tr>
</tbody>
</table>

Status: CVS Caremark Criteria
Type: Initial Prior Authorization
Ref # 1177-C

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

Fda-Approved Indications
Belsomra (suvorexant) is indicated for the treatment of insomnia characterized by difficulties with sleep onset and/or sleep maintenance.

Coverage Criteria
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of insomnia characterized by difficulties with sleep onset and/or sleep maintenance
  AND
- Potential causes of sleep disturbances have been addressed (e.g., inappropriate sleep hygiene and sleep environment issues or treatable medical/psychological causes of chronic insomnia)
  AND
- If the patient is less than 65 years of age, the patient experienced an inadequate treatment response, intolerance or contraindication to a generic non-benzodiazepine sedative-hypnotic (e.g., eszopiclone, zaleplon, zolpidem) OR a short/intermediate-acting benzodiazepine (e.g., temazepam, triazolam)

Quantity Limits apply.

Rationale
The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Belsomra (suvorexant) is indicated for the treatment of insomnia characterized by difficulties with sleep onset and/or sleep maintenance.

Insomnia disorder is defined in the International Classification of Sleep Disorders, Third Edition as a complaint of trouble initiating or maintaining sleep which is associated with daytime consequences and is not attributable to environmental circumstances or inadequate opportunity to sleep. The disorder is identified as chronic when it has persisted for at least three months at a frequency of at least three times per week. When the disorder meets the symptom criteria but has persisted for less than three months, it is considered short-term insomnia. Chronic insomnia, also referred to as “chronic insomnia disorder” in the American Psychiatric Association’s Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), is diagnosed according to the DSM-5 and the International Classification of Sleep Disorders, which have similar criteria for making the diagnosis. These criteria specify that symptoms must cause clinically significant functional distress or impairment; be present for at least three nights per week for at least three months; and not be linked to other sleep, medical, or mental disorders.
Insomnia can occur independently or be caused by another disease. According to the American Academy of Sleep Medicine (AASM), general treatment measures for insomnia include the treatment of comorbid medical and psychiatric conditions, modifying sleep-interfering medications and substances, and optimizing the sleep environment. The goal of treatment for insomnia is to improve sleep and alleviate distress or dysfunction caused by the disorder. Insomnia can be managed with psychological therapy, pharmacologic therapy, or a combination of both. Psychological therapy options include cognitive behavioral therapy for insomnia (CBT-I); multicomponent behavioral therapy or brief behavioral therapy (BBT) for insomnia; and other interventions such as stimulus control, relaxation strategies, and sleep restriction. Cognitive behavioral therapy for insomnia consists of a combination of cognitive therapy, behavioral interventions (such as sleep restriction and stimulus control), and educational interventions (such as sleep hygiene). The cognitive component is aimed at changing patient’s beliefs and attitudes about insomnia. Sleep hygiene education is often also included. The American College of Physicians (ACP) recommends that all adult patients receive CBT-I as the initial treatment for chronic insomnia disorder. Despite the clearly favorable benefit to risk ratio of CBT-I, not all patients with an insomnia disorder can and will derive benefit from this treatment alone.

The AASM Clinical Practice Guideline for the Pharmacological Treatment of Chronic Insomnia in Adults makes recommendations for treating sleep onset insomnia and sleep maintenance insomnia. Recommendations are not made for specific drugs over other drugs, rather the recommendations are made for treatment with a specific drug versus no treatment. The classes of drugs that received favorable recommendations include: orexin receptor agonists (suvorexant), non-benzodiazepine sedative hypnotics (eszopiclone, zaleplon, zolpidem), short/intermediate-acting benzodiazepines (triazolam and temazepam), melatonin agonists (ramelteon), and heterocyclics (Silenor [doxepin 3 mg, 6 mg]). Suvorexant is recommended for treating sleep maintenance insomnia as is Silenor. Triazolam, ramelteon, and zaleplon are recommended for the treatment of sleep onset insomnia. The guidelines recommend temazepam, eszopiclone, and zolpidem for the treatment of both sleep maintenance insomnia as well as sleep onset insomnia.

Because non-benzodiazepine sedative hypnotics and short/intermediate-acting benzodiazepines are the only drug classes recommended by the AASM for both sleep onset and sleep maintenance insomnia, coverage will be provided for Belsomra (suvorexant) in patients less than 65 years of age for the treatment of insomnia when an inadequate treatment response, intolerance or contraindication to a generic non-benzodiazepine sedative hypnotic (e.g., eszopiclone, zaleplon, zolpidem) or a short/intermediate-acting benzodiazepine (e.g., temazepam, triazolam) has been demonstrated.

Inappropriate drug prescribing can be defined as the use of medications whose risks outweigh the benefits. One common approach to this issue has been development of explicit “drugs-to-avoid” criteria. These criteria were initially developed by Dr. Mark H. Beers and later updated. Drugs-to-avoid lists include medications that should be avoided in any circumstance, doses that should not be exceeded, and drugs to avoid in patients with specific disorders. The National Committee for Quality Assurance (NCQA) assessed the Beers criteria as a quality indicator for ambulatory care. In 2002, NCQA convened a Medication Management Technical Subgroup. The NCQA has provided medication measures included in the U.S. Health Plan Employer Data and Information Set (HEDIS) as part of the standard assessment of quality in ambulatory care. NCQA and the Pharmacy Quality Alliance (PQA) utilize the American Geriatrics Society (AGS) Beers Criteria to designate the quality measure Use of High-Risk Medications in the Elderly (HRM). The Centers for Medicare and Medicaid Services (CMS) utilize the HRM measure to monitor and evaluate the quality of care provided to Medicare beneficiaries. NCQA additionally uses the AGS Beers Criteria to designate the quality measure Potentially Harmful Drug–Disease Interactions in the Elderly. In 2015, The American Geriatrics Society updated the Beers Criteria for Potentially Inappropriate Medications to Be Used with Caution with Older Adults. According to the 2015 update, and confirmed in the 2019 update, drug classes to avoid include short and intermediate acting benzodiazepines and benzodiazepine receptor agonists. Older adults have increased sensitivity to benzodiazepines; benzodiazepines increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle crashes. Benzodiazepine receptor agonists have adverse reactions similar to those of benzodiazepines in older adults (e.g., delirium, falls, fractures); increased emergency department visits and hospitalizations; motor vehicle crashes; minimal improvement in sleep latency and duration. Therefore, a trial of a generic non-benzodiazepine sedative hypnotic (e.g., eszopiclone, zaleplon, zolpidem) or a short/intermediate-acting benzodiazepine (e.g., temazepam, triazolam) will not be required for patients 65 years of age or older.
The recommended dose for Belsomra (suvorexant) is 10 mg, taken no more than once per night and within 30 minutes of going to bed, with at least 7 hours remaining before the planned time of awakening. If the 10 mg dose is well-tolerated but not effective, the dose can be increased. The maximum recommended dose of Belsomra (suvorexant) is 20 mg once daily. It is recommended to use the lowest effective dose for the patient. Belsomra (suvorexant) is available as 5 mg, 10 mg, 15 mg, and 20 mg tablets.

Belsomra (suvorexant) is supplied in unit-of-use blisters of 30 tablets. Due to the possibility of the package not being split at the time of dispensing, Belsomra (suvorexant) is not included in the Insomnia Limit criteria.

REFERENCES
**CRITERIA FOR APPROVAL**

1. Is the requested drug being prescribed for the treatment of insomnia characterized by difficulties with sleep onset and/or sleep maintenance?  
   - Yes  
   - No

2. Have potential causes of sleep disturbances been addressed (e.g., inappropriate sleep hygiene and sleep environment issues or treatable medical/psychological causes of chronic insomnia)?  
   - Yes  
   - No

3. Is the patient 65 years of age or older?  
   - Yes  
   - No  
   *[If yes, then skip to question 5.]*

4. Has the patient experienced an inadequate treatment response, intolerance or contraindication to a generic non-benzodiazepine sedative-hypnotic (e.g., eszopiclone, zaleplon, zolpidem) OR a short/intermediate-acting benzodiazepine (e.g., temazepam, triazolam)?  
   - Yes  
   - No

5. Does the patient require use of MORE than the plan allowance of 30 tablets per month of Belsomra (suvorexant)?  
   - Yes  
   - No  
   *[RPh Note: If yes, then deny and enter a partial approval for 30 tablets per 25 days or 90 tablets per 75 days]*

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**Mapping Instructions**

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
<th>DENIAL REASONS – DO NOT USE FOR MEDICARE PART D</th>
</tr>
</thead>
</table>
| 1. Go to 2 | Deny | You do not meet the requirements of your plan. Your plan covers this drug when you have insomnia. Your request has been denied based on the information we have.  
   *[Short Description: No approvable diagnosis]* |
| 2. Go to 3 | Deny | You do not meet the requirements of your plan. Your plan covers this drug when reasons for insomnia have been addressed. Your request has been denied based on the information we have.  
   *[Short Description: No confirmation that causes of sleep disturbances have been addressed]* |
| 3. Go to 5 | Go to 4 | |
| 4. Go to 5 | Deny | You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions:  
   - You are 64 years of age or younger  
   - You tried another drug for insomnia first (generic non-benzodiazepine sedative-hypnotic such as eszopiclone, zaleplon, zolpidem OR a short/intermediate-acting benzodiazepine such as temazepam, triazolam)  
   - The other drugs did not work for you or you cannot use them  
   Your request has been denied based on the information we have.  
   *[Short Description: Less than 65 years of age and no inadequate response, intolerance or contraindication a generic non-benzodiazepine sedative-hypnotic OR a short acting benzodiazepine]* |
| 5. | Deny | Approve, 36 months 30 tablets/25 days* or 90 tablets/75 days* to accumulate across all strengths | You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 30 tablets/month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity] |

*The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*
PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Insomnia Agents</th>
</tr>
</thead>
</table>

**Brand Name**

<table>
<thead>
<tr>
<th>(Generic)</th>
</tr>
</thead>
</table>

- **Edluar Sublingual Tablets**
  - (zolpidem)
- **Intermezzo Sublingual Tablets**
  - (zolpidem)
- **Zolpimist Oral Spray**
  - (zolpidem)

**Status: CVS Caremark Criteria**
**Type: Initial Prior Authorization**

*Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

**FDA-Approved Indications**

**Edluar**

Edluar sublingual tablets are indicated for the short-term treatment of insomnia characterized by difficulties with sleep initiation. The clinical trials performed with Edluar in support of efficacy were 4-5 weeks in duration with the final formal assessments of sleep latency performed at the end of treatment.

**Intermezzo**

Intermezzo sublingual tablet is indicated for use as needed for the treatment of insomnia when a middle-of-the-night awakening is followed by difficulty returning to sleep.

Limitations of Use: Intermezzo is not indicated for the treatment of middle-of-the-night insomnia when the patient has fewer than 4 hours of bedtime remaining before the planned time of waking.

**Zolpimist**

Zolpimist oral spray is indicated for the short-term treatment of insomnia characterized by difficulties with sleep initiation. Zolpimist has been shown to decrease sleep latency for up to 35 days in controlled clinical studies. The clinical trials performed in support of efficacy were 4-5 weeks in duration with the final formal assessment of sleep latency performed at the end of treatment.

**Coverage Criteria**

Zolpimist (zolpidem) oral spray and Edluar (zolpidem) sublingual tablets

The requested drug will be covered with prior authorization when the following criteria are met:

- The drug is being prescribed for insomnia characterized by difficulties with sleep initiation AND
- Potential causes of sleep disturbances have been addressed (e.g., inappropriate sleep hygiene and sleep environment issues or treatable medical/psychological causes of chronic insomnia) AND
- The patient is unable to swallow tablets/capsules

Insomnia Agents (Edluar, Intermezzo, Zolpimist) 387-C 03-2019

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OR

Intermezzo (zolpidem) sublingual tablets

The requested drug will be covered with prior authorization when the following criteria are met:

- The drug is being prescribed for insomnia when middle-of-the-night awakening is followed by difficulty returning to sleep
- AND
- Potential causes of sleep disturbances have been addressed (e.g., inappropriate sleep hygiene and sleep environment issues or treatable medical/psychological causes of chronic insomnia)
- AND
- The patient is one of the following: biological male or a person that self-identifies as a male, 65 years of age and under, or not taking the requested drug concomitantly with other CNS depressants (e.g., benzodiazepines, opioids, tricyclic antidepressants, alcohol)

OR

- The patient is one of the following: biological female or a person that self-identifies as a female, over 65 years old or taking the requested drug concomitantly with other CNS depressants (e.g., benzodiazepines, opioids, tricyclic antidepressants, alcohol)
  - AND
  - The request is for the 1.75 mg strength

Quantity Limits apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Edluar (zolpidem) and ZolpiMist (zolpidem) are indicated for the short-term treatment of insomnia characterized by difficulties with sleep initiation. ZolpiMist (zolpidem) oral spray and Edluar (zolpidem) sublingual tablets are an alternative treatment for patients who are unable to swallow tablets/capsules.

Intermezzo (zolpidem) is indicated for use as needed for the treatment of insomnia when a middle-of-the-night awakening is followed by difficulty returning to sleep. Intermezzo (zolpidem) is not indicated for the treatment of middle-of-the-night insomnia when the patient has fewer than 4 hours of bedtime remaining before the planned time of waking. Intermezzo (zolpidem) will be considered for coverage for patients who have middle-of-the-night awakening followed by difficulty returning to sleep and when other potential causes of sleep disturbances have been addressed.

Insomnia disorder is defined in the International Classification of Sleep Disorders, Third Edition as a complaint of trouble initiating or maintaining sleep which is associated with daytime consequences and is not attributable to environmental circumstances or inadequate opportunity to sleep. The disorder is identified as chronic when it has persisted for at least three months at a frequency of at least three times per week. When the disorder meets the symptom criteria but has persisted for less than three months, it is considered short-term insomnia. Chronic insomnia, also referred to as “chronic insomnia disorder” in the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), is diagnosed according to the DSM-5 and the International Classification of Sleep Disorders, which have similar criteria for making the diagnosis. These criteria specify that symptoms must cause clinically significant functional distress or impairment; be present for at least three nights per week for at least three months; and not be linked to other sleep, medical, or mental disorders.

Insomnia disorder is defined in the International Classification of Sleep Disorders, Third Edition as a complaint of trouble initiating or maintaining sleep which is associated with daytime consequences and is not attributable to environmental circumstances or inadequate opportunity to sleep. The disorder is identified as chronic when it has persisted for at least three months at a frequency of at least three times per week. When the disorder meets the symptom criteria but has persisted for less than three months, it is considered short-term insomnia. Chronic insomnia, also referred to as “chronic insomnia disorder” in the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), is diagnosed according to the DSM-5 and the International Classification of Sleep Disorders, which have similar criteria for making the diagnosis. These criteria specify that symptoms must cause clinically significant functional distress or impairment; be present for at least three nights per week for at least three months; and not be linked to other sleep, medical, or mental disorders.

Insomnia can occur independently or be caused by another disease. According to the American Academy of Sleep Medicine (AASM), general treatment measures for insomnia include the treatment of comorbid medical and psychiatric conditions, modifying sleep-interfering medications and substances, and optimizing the sleep environment. The goal of treatment for insomnia is to improve sleep and alleviate distress or dysfunction caused by the disorder. Insomnia can be managed with psychological therapy, pharmacologic therapy, or a combination of both. Psychological therapy options include cognitive behavioral therapy for insomnia (CBT-I); multicomponent behavioral therapy or brief behavioral therapy (BBT) for insomnia; and other interventions such as stimulus control, relaxation strategies, and sleep restriction. Cognitive therapy options include cognitive behavioral therapy for insomnia (CBT-I); multicomponent behavioral therapy or brief behavioral therapy (BBT) for insomnia; and other interventions such as stimulus control, relaxation strategies, and sleep restriction. Cognitive...
behavioral therapy for insomnia consists of a combination of cognitive therapy, behavioral interventions (such as sleep restriction and stimulus control), and educational interventions (such as sleep hygiene). The cognitive component is aimed at changing patient’s beliefs and attitudes about insomnia. Sleep hygiene education is often also included.8-10 The American College of Physicians (ACP) recommends that all adult patients receive cognitive CBT-I as the initial treatment for chronic insomnia disorder.8 Despite the clearly favorable benefit to risk ratio of CBT-I, not all patients with an insomnia disorder can and will derive benefit from this treatment alone.8,9

The recommended initial dose of Edluar (zolpidem) and ZolpiMist (zolpidem) is 5 mg for women and either 5 or 10 mg for men, taken only once per night immediately before bedtime with at least 7-8 hours remaining before the planned time of awakening. If the 5 mg dose is not effective, the dose can be increased to 10 mg. In some patients, the higher morning blood levels following use of the 10 mg dose increase the risk of next day impairment of driving and other activities that require full alertness. The total dose of Edluar (zolpidem) or ZolpiMist (zolpidem) should not exceed 10 mg once daily immediately before bedtime. The recommended doses for women and men are different because zolpidem clearance is lower in women. It is recommended to use the lowest effective dose for the patient.

The recommended and maximum dose of Intermezzo (zolpidem) is 1.75 mg for women and 3.5 mg for men, taken only once per night as needed if a middle-of-the-night awakening is following by difficulty returning to sleep. The recommended doses for women and men are different because women clear zolpidem from the body at a lower rate than men. The recommended dose of Intermezzo (zolpidem) in men and women over 65 years of age is 1.75 mg. The recommended dose for patients who are taking concomitant CNS depressants (e.g., benzodiazepines, opioids, tricyclic antidepressants, alcohol) is also 1.75 mg.

REFERENCES
### CRITERIA FOR APPROVAL

1. Have potential causes of sleep disturbances been addressed (e.g., inappropriate sleep hygiene and sleep environment issues or treatable medical/psychological causes of chronic insomnia)?
   - Yes
   - No

2. Is the request for ZolpiMist (zolpidem) oral spray or Edluar (zolpidem) sublingual tablets?
   - Yes
   - No
   [If no, then skip to question 6.]

3. Is the requested drug being prescribed for insomnia characterized by difficulties with sleep initiation?
   - Yes
   - No

4. Is the patient unable to swallow tablets/capsules?
   - Yes
   - No

5. Does the patient require use of MORE than 30 tablets per month of Edluar (zolpidem) sublingual tablets or 1 container of ZolpiMist (zolpidem) oral spray?
   - Yes
   - No
   [No further questions.]
   [RPh Note: If yes, then deny and enter a partial approval for 30 tablets per 25 days or 90 tablets per 75 days of Edluar (zolpidem) sublingual tablets or 1 container per 25 days or 3 containers per 75 days of ZolpiMist (zolpidem) oral spray.]

6. Is the requested drug being prescribed for insomnia when middle-of-the-night awakening is followed by difficulty returning to sleep?
   - Yes
   - No

7. Is the patient one of the following: A) biological female or a person that self-identifies as a female, B) over 65 years old, C) taking the requested drug concomitantly with other CNS depressants (e.g., benzodiazepines, opioids, tricyclic antidepressants, alcohol)?
   - Yes
   - No
   [If yes, then go to question 9.]

8. Does the patient require use of MORE than 30 tablets per month of Intermezzo (zolpidem) sublingual tablets 1.75 mg or 3.5 mg?
   - Yes
   - No
   [No further questions.]
   [RPh Note: If yes, then deny and enter a partial approval for 30 tablets per 25 days or 90 tablets per 75 days of Intermezzo (zolpidem) sublingual tablets 1.75 mg or 3.5 mg.]

9. Is the request for the 1.75 mg strength for a dose not exceeding 1.75 mg per day?
   - Yes
   - No

10. Does the patient require use of MORE than 30 tablets per month of Intermezzo (zolpidem) sublingual tablets 1.75 mg?
    - Yes
    - No
    [RPh Note: If yes, then deny and enter a partial approval for 30 tablets per 25 days or 90 tablets per 75 days of Intermezzo (zolpidem) sublingual tablets 1.75 mg.]
<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
<th>DENIAL REASONS – DO NOT USE FOR MEDICARE PART D</th>
</tr>
</thead>
</table>
| 1. | Go to 2 | Deny | You do not meet the requirements of your plan. Your plan covers this drug when reasons for insomnia have been addressed. Your request has been denied based on the information we have.  
[Short Description: No confirmation that causes of sleep disturbances have been addressed] |
| 2. | Go to 3 | Go to 6 | |
| 3. | Go to 4 | Deny | You do not meet the requirements of your plan. Your plan covers this drug when you have difficulty falling asleep. Your request has been denied based on the information we have.  
[Short Description: No approvable diagnosis] |
| 4. | Go to 5 | Deny | You do not meet the requirements of your plan. Your plan covers this drug when you are unable to swallow tablets/capsules. Your request has been denied based on the information we have.  
[Short Description: No confirmation dosage form required] |
| 5. | Deny | Approve, 36 months   
Edluar - 30 sublingual tabs/25* days or 90 sublingual tabs/75 days* or ZolpiMist - 1 container/25 days* or 3 containers/75 days* | You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:  
- 30 tablets per month of Edluar (zolpidem sublingual tablets) or  
- 1 container per month of ZolpiMist (zolpidem oral spray)  
You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied.  
[Short Description: Over max quantity] |
| 6. | Go to 7 | Deny | You do not meet the requirements of your plan. Your plan covers this drug when you have middle-of-the-night awakening. Your request has been denied based on the information we have.  
[Short Description: No approvable diagnosis] |
| 7. | Go to 9 | Go to 8 | |
| 8. | Deny | Approve, 36 months   
Intermezzo 1.75 mg – 30 sublingual tabs/25 days* or 90 sublingual tabs/75 days*   
Intermezzo 3.5 mg – 30 sublingual tabs*/25 days or 90 sublingual tabs/75 days* | You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 30 tablets per month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied.  
[Short Description: Over max quantity] |
| 9. | Go to 10 | Deny | You do not meet the requirements of your plan. Your plan covers this drug if you meet one of the following:  
- You are a biological female or a person that self-identifies as a female  
- You are over 65 years old  
- You are taking this drug at the same time as another CNS depressants (e.g., benzodiazepines, opioids, tricyclic antidepressants, alcohol) AND |
<p>| | | |</p>
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</table>
| **10.** | **Deny** | - You are not taking more than 1.75 mg per day Your request has been denied based on the information we have.  
[Short Description: Over max approvable dose] |

<p>| | | |</p>
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</table>
| **Approve, 36 months Intermezzo 1.75 mg Only– 30 sublingual tabs/25 days* or 90 sublingual tabs/75 days*** | - You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 30 tablets/month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied.  
[Short Description: Over max quantity] |

*The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*
SPECIALTY GUIDELINE MANAGEMENT

INTRON A (interferon alfa-2b)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Malignant melanoma
   2. Condylomata acuminata
   3. Hairy cell leukemia
   4. AIDS-related Kaposi sarcoma
   5. Chronic hepatitis B virus infection
   6. Chronic hepatitis C virus infection
   7. Follicular non-Hodgkin’s lymphoma

B. Compendial Uses
   1. Non-Hodgkin’s lymphoma
      i. Adult T-cell leukemia/lymphoma (ATLL)
      ii. Mycosis fungoides (MF)/Sezary syndrome (SS)
   2. Myeloproliferative neoplasms
      i. Essential thrombocythemia
      ii. Myelofibrosis
      iii. Polycythemia vera
   3. Renal cell carcinoma
   4. Chronic myelogenous leukemia (CML)
   5. Giant cell tumor of the bone
   6. Acute hepatitis C virus infection
   7. Desmoid tumors (soft tissue sarcoma)
   8. Systemic mastocytosis
   9. Carcinoid syndrome
   10. Hypereosinophilic syndrome
   11. Kasabach-Merritt syndrome
   12. Leptomeningeal metastases
   13. Life threatening hemangioma of infancy
   14. Meningeoma
   15. Neuroendocrine tumors of the GI tract, lung, or thymus (carcinoid tumors)
   16. Ocular surface neoplasia (conjunctival and corneal neoplasm)
   17. Respiratory papillomatosis
   18. Vulvar vestibulitis

All other indications are considered experimental/investigational and are not a covered benefit.
II. CRITERIA FOR INITIAL APPROVAL

A. Malignant melanoma
   Authorization of 12 months may be granted for treatment of malignant melanoma.

B. Non-Hodgkin’s lymphoma (NHL)
   Authorization of 12 months may be granted for treatment of NHL with any of the following subtypes:
   1. Adult T-cell leukemia/lymphoma (ATLL) when used in combination with either of the following:
      a. Zidovudine, or
      b. Arsenic trioxide
   2. Mycosis fungoides (MF)/Sezary syndrome (SS)
   3. Hairy cell leukemia when used as a single agent
   4. Follicular lymphoma (clinically aggressive)

C. Renal cell carcinoma
   Authorization of 12 months may be granted for treatment of renal cell carcinoma when both of the following criteria are met:
   1. Intron-A will be used in combination with bevacizumab.
   2. The disease is of clear-cell histology.

D. Condylomata acuminata
   Authorization of 12 months may be granted for treatment of condylomata acuminata.

E. AIDS-related Kaposi sarcoma
   Authorization of 12 months may be granted for treatment of AIDS-related Kaposi sarcoma when both of the following criteria are met:
   1. Intron-A is used for subsequent therapy.
   2. Intron-A will be given with antiretroviral therapy (ART).

F. Chronic myelogenous leukemia (CML)
   Authorization of 6 months may be granted for treatment of CML.

G. Giant cell tumor of the bone
   Authorization of 12 months may be granted for treatment of giant cell tumor of the bone when either of the following criteria are met:
   1. Intron-A will be used as a single agent, or
   2. Intron-A will be used in combination with denosumab.

H. Desmoid tumors (soft tissue sarcoma)
   Authorization of 12 months may be granted for treatment of desmoid tumors when used as a single agent.

I. Acute and chronic hepatitis C virus infection
   Authorization of up to 48 weeks may be granted for treatment of acute and chronic hepatitis C virus infection.

J. Chronic hepatitis B (including hepatitis D virus co-infection) virus infection
   Authorization of 48 weeks may be granted for treatment of chronic hepatitis B (including hepatitis D virus co-infection) virus infection.

K. Myeloproliferative neoplasms
   Authorization of 12 months may be granted for treatment of symptomatic low-risk myelofibrosis, essential thrombocythemia, and polycythemia vera.
L. **Systemic mastocytosis**
   Authorization of 12 months may be granted for treatment of systemic mastocytosis when either of the following criteria are met:
   1. Intron-A will be used as a single agent, or
   2. Intron-A will be used in combination with prednisone.

M. **Hypereosinophilic syndrome**
   Authorization of 12 months may be granted for treatment of hypereosinophilic syndrome when the patient has had an inadequate response or has contraindication to corticosteroids.

N. **Kasabach-Merritt syndrome**
   Authorization of 12 months may be granted for treatment of Kasabach-Merritt syndrome.

O. **Leptomeningeal metastases**
   Authorization of 12 months may be granted for treatment of leptomeningeal metastases.

P. **Life threatening hemangioma of infancy**
   Authorization of 12 months may be granted for treatment of life threatening hemangioma in an infant patient who has had an inadequate response or contraindication to corticosteroids.

Q. **Meningeoma**
   Authorization of 12 months may be granted for treatment of meningioma when either of the following criteria are met:
   1. The disease is recurrent, or
   2. The disease is surgically inaccessible.

R. **Neuroendocrine tumors of the GI tract, lung, or thymus (carcinoid tumors)**
   Authorization of 12 months may be granted for treatment of neuroendocrine tumors of the GI tract, lung, or thymus.

S. **Carcinoid syndrome**
   Authorization of 12 months may be granted for treatment of carcinoid syndrome.

T. **Ocular surface neoplasia (conjunctival and corneal neoplasm)**
   Authorization of 12 months may be granted for treatment of ocular surface neoplasia (conjunctival and corneal neoplasm).

U. **Respiratory papillomatosis**
   Authorization of 12 months may be granted for treatment of respiratory papillomatosis.

V. **Vulvar vestibulitis**
   Authorization of 12 months may be granted for treatment of vulvar vestibulitis

III. **CONTINUATION OF THERAPY**

   Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. **REFERENCES**
SPECIALTY GUIDELINE MANAGEMENT

IRESSA (gefitinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Iressa is indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test.

Limitation of Use: Safety and efficacy of Iressa have not been established in patients who have EGFR mutations other than exon 19 deletions or exon 21 (L858R) substitution mutations.

B. Compendial Use

1. EGFR mutation-positive recurrent, advanced, or metastatic NSCLC
2. Brain metastases from sensitizing EGFR mutation-positive NSCLC

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: EGFR mutation testing results.

III. CRITERIA FOR INITIAL APPROVAL

Non-small cell lung cancer (NSCLC)

Authorization of 12 months may be granted for treatment of recurrent, advanced, or metastatic NSCLC (including brain metastases from NSCLC) in members with sensitizing EGFR mutation-positive disease.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced an unacceptable toxicity.

V. REFERENCES

PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
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</thead>
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<tr>
<td>ABSORICA (isotretinoin)</td>
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<td>AMNESTEEM (isotretinoin)</td>
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<td>CLARAVIS (isotretinoin)</td>
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<tr>
<td>MYORISAN (isotretinoin)</td>
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<tr>
<td>ZENATANE (isotretinoin)</td>
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</tbody>
</table>

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

**FDA-APPROVED INDICATIONS**

Isotretinoin is indicated for the treatment of severe recalcitrant nodular acne. Nodules are inflammatory lesions with a diameter of 5 mm or greater. The nodules may become suppurative or hemorrhagic. “Severe,” by definition, means “many” as opposed to “few or several” nodules. Because of significant adverse effects associated with its use, isotretinoin should be reserved for patients with severe nodular acne who are unresponsive to conventional therapy, including systemic antibiotics. In addition, isotretinoin is indicated only for those female patients who are not pregnant, because isotretinoin can cause severe birth defects.

A single course of therapy for 15 to 20 weeks has been shown to result in complete and prolonged remission of disease in many patients. If a second course of therapy is needed, it should not be initiated until at least 8 weeks after completion of the first course, because experience has shown that patients may continue to improve while off isotretinoin. The optimal interval before retreatment has not been defined for patients who have not completed skeletal growth.

**Compendial Uses**

- Acne – refractory
- Cutaneous T-cell Lymphoma (CTCL) (e.g., mycosis fungoides, Sézary syndrome)
- Keratosis follicularis (Darier Disease) – severe
- Lamellar ichthyosis – severe skin involvement
- Neuroblastoma
- Pityriasis rubra pilaris
- Rosacea – severe refractory
- Squamous Cell Cancers – to reduce the development of precancers and skin cancers in high risk patients
-Transient acantholytic dermatosis (Grover’s Disease) – severe
COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has any of the following diagnoses: A) severe recalcitrant nodular acne vulgaris, B) refractory acne vulgaris, C) severe refractory rosacea

AND

- The patient has tried and had an inadequate treatment responses to any topical acne product AND an oral antibiotic

AND

- Treatment will be limited to 40 weeks (2 courses) or less AND with at least 8 weeks between each course

OR

- The patient has any of the following diagnoses: A) neuroblastoma, B) cutaneous T-cell lymphoma (CTCL) (e.g., mycosis fungoides, Sézary syndrome), C) is at high risk for developing skin cancer (squamous cell cancers), D) transient acantholytic dermatosis (Grover's Disease), E) keratosis follicularis (Darier Disease), F) lamellar ichthyosis, G) pityriasis rubra pilaris

RATIONALE
The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Isotretinoin is indicated for the treatment of severe recalcitrant nodular acne. Nodules are inflammatory lesions with a diameter of 5 mm or greater. The nodules may become suppurative or hemorrhagic. “Severe,” by definition, means “many” as opposed to “few or several” nodules. Because of significant adverse effects associated with its use, isotretinoin should be reserved for patients with severe nodular acne who are unresponsive to conventional therapy, including systemic antibiotics. In addition, isotretinoin is indicated only for those female patients who are not pregnant, because isotretinoin can cause severe birth defects.

A single course of therapy for 15 to 20 weeks has been shown to result in complete and prolonged remission of disease in many patients. If a second course of therapy is needed, it should not be initiated until at least 8 weeks after completion of the first course, because experience has shown that patients may continue to improve while off isotretinoin. The optimal interval before retreatment has not been defined for patients who have not completed skeletal growth. Long-term use of isotretinoin even in low doses, has not been studied, and is not recommended. It is important that isotretinoin be given at the recommended doses for no longer than the recommended duration. The effect of long-term use of isotretinoin on bone loss is unknown.

Patients with acne vulgaris may be treated with antibacterial, keratolytic, retinoid, or antibiotic topical products (e.g., salicylic acid, benzoyl peroxide, azelaic acid, adapalene, tretinoin, tazarotene, clindamycin, erythromycin). Combinations of products, if compatible, may be used when monotherapy is inadequate. Systemic antibiotics are a standard of care in the management of moderate and severe acne and treatment-resistant forms of inflammatory acne. There is evidence to support the use of tetracycline, doxycycline, minocycline, erythromycin, trimethoprim-sulfamethoxazole, trimethoprim, and azithromycin. For patients with severe inflammatory acne that does not improve with other medications, isotretinoin may be prescribed. The compendia state that isotretinoin is effective in treating acne, however, should be reserved for patients who are unresponsive to conventional acne therapies, including oral and/or topical anti-infectives.

The National Cancer Institute states that patients with neuroblastoma categorized as high risk are generally treated with dose-intensive multiagent chemotherapy, resection of the primary tumor, followed by myeloablative chemotherapy and autologous stem cell transplantation. Radiation of residual tumor and original sites of metastases is often performed. After recovery, patients are treated with oral isotretinoin for 6 months. Both myeloablative chemotherapy and isotretinoin improve outcome in patients categorized as high risk.

The National Comprehensive Cancer Network (NCCN) guidelines state that certain patient groups are at high risk for developing multiple squamous cell skin cancers and tumors that can behave aggressively. These include organ transplant recipients, other settings of immunosuppression (e.g., lymphoma, drug-induced, HIV), xeroderma pigmentosum. Use of oral retinoids (acitretin, isotretinoin) has been effective in reducing the development of precancers.
and skin cancers in some high risk patients. Side effects may be significant. Therapeutic effects disappear shortly after cessation of the drug. 6,7,13,15

The NCCN guidelines also state that retinoids (all-trans retinoic acid, 13-cis retinoic acid and their synthetic analogs acitretin and isotretinoin) and interferons have been used for many years in the treatment of cutaneous T-cell lymphoma (CTCL; e.g., mycosis fungoides, Sézary syndrome). 6,7,14,15

Isotretinoin has been used in the treatment of rosacea, transient acantholytic dermatosis (Grover’s Disease), keratosis follicularis (Darier Disease), lamellar ichthyosis, and pityriasis rubra pilaris that are resistant to treatment with other agents; however, the specific role of isotretinoin in the treatment of these disorders and the safety of long-term use and high dosages of the drug have not been determined. In order to limit total isotretinoin dosage, isotretinoin should be used only if the disease is severe, the dosage is as low as possible and given intermittently, and should be combined with other topical therapy. 6,7

Based on the results of several studies, the compendia favor efficacy for isotretinoin in treating severe, refractory rosacea at a preferred dose of 0.05mg/kg/day for approximately 2 to 6 months of treatment. The National Institute of Arthritis and Musculoskeletal and Skin Diseases states that rosacea can be treated and controlled with a topical antibiotic. Topical keratolytics such as benzoyl peroxide and azelaic acid offer limited symptomatic control of inflammatory pustules. In addition, topical metronidazole may be helpful for mild disease and in addition to systemic therapy. For people with more severe cases oral antibiotics are often prescribed. Long-term, low-dose isotretinoin may be helpful for recalcitrant disease for some patients.6,7,10,11

For transient acantholytic dermatosis (Grover’s Disease), treatment is usually based on a person's symptoms. Initial treatment options include topical steroids, topical antihistamines, or topical selenium sulfide. For more severe cases, tetracycline has been reported to be effective and the use of oral retinoids (acetretin or isotretinoin) has been reported. More troubling eruptions usually clear up after taking isotretinoin or tetracycline for one to three months.6,7,16-18

For keratosis follicularis (Darier Disease), moisturizers with urea or lactic acid can help reduce scaling and thickening of the lesions. Low to medium potency topical steroids are sometimes useful for reducing inflammation and when bacterial growth is suspected, application of antiseptics can be helpful. Topical retinoids have been shown to be effective in reducing the localized symptoms of this disease in 3 months. The most effective medical treatment for severe cases has been the use oral retinoids such as acitretin and isotretinoin.6,7,19,20

For lamellar ichthyosis, petrolatum-based creams and ointments are used to keep the skin soft. As affected children become older, keratolytic agents such as alpha-hydroxy acid or urea preparations may be used to promote peeling and thinning of the stratum corneum. For individuals with ectropion, lubrication of the cornea with artificial tears or prescription ointments is helpful in preventing drying out of the cornea. Oral retinoid therapy such as acitretin or isotretinoin may be recommended for those with severe skin involvement to help increase the patient’s ability to perspire, improve the ectropion, and reduce the severity of erythema, scaling, induration, and crusting.6,7,21

Management of pityriasis rubra pilaris (PRP) often involves systemic and topical therapies combined. Topical therapies can help with the symptoms and may be enough for people with mild PRP. Topical treatments used for PRP may include topical corticosteroids, keratolytics, tar, calcipotriol, topical tretinoin, and tazarotene. Topical treatments are usually combined with systemic therapy for PRP that affects a large part of the body. Oral retinoids (synthetic vitamin A derivatives) are usually preferred as a first-line systemic treatment. Methotrexate may be an alternative option for people who should not use systemic retinoids, or who don't respond to systemic retinoid therapy. For people who don't respond well to retinoid or methotrexate therapy, options may include biologic TNF-alpha inhibitors, azathioprine, cyclosporine, and/or phototherapy. 6,7,22,23

REFERENCES
CRITERIA FOR APPROVAL

1. Does the patient have any of the following diagnoses: A) severe recalcitrant nodular acne vulgaris, B) refractory acne vulgaris, C) severe refractory rosacea? 
   [If no, then skip to question 4.]
   Yes  No

2. Has the patient tried and had an inadequate treatment responses to any topical acne product AND an oral antibiotic?
   [Note: topical products include salicylic acid, benzoyl peroxide, azelaic acid, adapalene, tretinoin, tazarotene, clindamycin, erythromycin, or metronidazole for rosacea]
   [Note: oral antibiotics include minocycline, doxycycline, tetracycline, erythromycin, trimethoprim-sulfamethoxazole, trimethoprim, azithromycin]
   Yes  No

3. Will treatment be limited to 40 weeks (2 courses) or less AND with at least 8 weeks between each course? 
   [No further questions.]
   Yes  No

4. Does the patient have any of the following diagnoses: A) neuroblastoma, B) cutaneous T-cell lymphoma (CTCL) (e.g., mycosis fungoides, Sezary syndrome), C) is at high risk for developing skin cancer (squamous cell cancers), D) transient acantholytic dermatosis (Grover’s Disease), E) keratosis follicularis (Darier Disease), F) lamellar ichthyosis, G) pityriasis rubra pilaris?
   Yes  No

Guidelines for Approval

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<td>2</td>
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Mapping Instructions

<table>
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<th>DENIAL REASONS – DO NOT USE FOR MEDICARE PART D</th>
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<tbody>
<tr>
<td>1.</td>
<td>Go to 2</td>
<td>Go to 4</td>
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<tr>
<td>2.</td>
<td>Go to 3</td>
<td>Deny</td>
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<tr>
<td></td>
<td></td>
<td>You do not meet the requirements of your plan.</td>
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<td></td>
<td>Your plan covers this drug when you meet all of these conditions:</td>
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<td>- You tried another topical acne product first, which did not work for you</td>
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<td></td>
<td>- You tried an oral antibiotic first, which did not work for you</td>
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<td></td>
<td>Your request has been denied based on the information we have.</td>
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<tr>
<td></td>
<td></td>
<td>[Short Description: No trial of topical acne products and oral antibiotics]</td>
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<td>3.</td>
<td>Approve, 12 Months</td>
<td>Deny</td>
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<tr>
<td></td>
<td></td>
<td>You do not meet the requirements of your plan.</td>
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<td>Your plan covers this drug when you meet all of the following conditions:</td>
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<td>- You will not use it for more than 40 weeks (2 treatment courses)</td>
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<td></td>
<td>- You will take an 8-week break between treatment courses</td>
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<td>Your request has been denied based on the information we have.</td>
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<td>[Short Description: Over max duration of use]</td>
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<td>4.</td>
<td>Approve, 12 Months</td>
<td>Deny</td>
</tr>
<tr>
<td></td>
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<td>You do not meet the requirements of your plan.</td>
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<tr>
<td></td>
<td></td>
<td>Your plan covers this drug when you meet one of these conditions:</td>
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<tr>
<td></td>
<td></td>
<td>- You have severe recalcitrant nodular acne vulgaris</td>
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<td></td>
<td></td>
<td>- You have severe refractory acne vulgaris</td>
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<tr>
<td></td>
<td></td>
<td>- You have severe refractory rosacea</td>
</tr>
<tr>
<td></td>
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<td>- You have neuroblastoma</td>
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Isotretinoin 118-A 06-2019 ©2019 CVS Caremark. All rights reserved.

This document contains confidential and proprietary information of CVS Caremark and cannot be reproduced, distributed or printed without written permission from CVS Caremark. This document contains references to brand-name prescription drugs that are trademarks or registered trademarks of pharmaceutical manufacturers not affiliated with CVS Caremark.
- You have cutaneous T-cell lymphoma
- You are at high risk for developing skin cancer
- You have transient acantholytic dermatosis (Grover’s Disease)
- You have keratosis follicularis (Darier Disease)
- You have lamellar ichthyosis
- You have pityriasis rubra pilaris

Your request has been denied based on the information we have.
[Short Description: No approvable diagnosis]
SPECIALTY GUIDELINE MANAGEMENT

ISTODAX (romidepsin)

POLICY

I. INDICATIONS
The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Cutaneous T-cell lymphoma (CTCL) in patients who have received at least one prior systemic therapy
   2. Peripheral T-cell lymphoma (PTCL) in patients who have received at least one prior therapy

B. Compendial Uses
   1. Mycosis fungoides (MF)
   2. Sézary syndrome (SS)

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR APPROVAL

A. Cutaneous T-cell lymphoma (CTCL)
   Authorization of 12 months may be granted for the treatment of CTCL (e.g., mycosis fungoides, Sézary syndrome).

B. Peripheral T-cell lymphoma (PTCL) (see Appendix for examples of PTCL subtypes)
   Authorization of 12 months may be granted for the treatment of PTCL.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria.

IV. APPENDIX: Examples of PTCL subtypes

1. Peripheral T-cell lymphoma not otherwise specified (PTCL-NOS)
2. Angioimmunoblastic T-cell lymphoma (AITL)
3. Anaplastic large cell lymphoma (ALCL), anaplastic lymphoma kinase (ALK)+/ALK-
4. Primary cutaneous anaplastic large cell lymphoma (PC-ALCL)
5. Enteropathy-associated T-cell lymphoma (EATL)
6. Adult T-cell leukemia/lymphoma (ATLL)
7. Monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL)
8. Nodal peripheral T-cell lymphoma with TFH phenotype (PTCL, TFH)
9. Follicular T-cell lymphoma (FTCL)
10. Extranodal NK/T-cell lymphoma, nasal type (ENKL)
11. Hepatosplenic gamma-delta-T-cell lymphoma (HSGDTCL)

REFERENCES
PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>BRAND NAME* (generic)</th>
<th>ONMEL (itraconazole tablets)</th>
</tr>
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<tr>
<td>Status: CVS Caremark Criteria</td>
<td>MDC-1</td>
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<td>Ref # 919-A</td>
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* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS
Onmel is indicated for the treatment of onychomycosis of the toenail due to *Trichophyton rubrum* or *T. mentagrophytes* in non-immunocompromised patients. Prior to initiating treatment, appropriate nail specimens for laboratory testing (KOH preparation, fungal culture, or nail biopsy) should be obtained to confirm the diagnosis of onychomycosis.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of onychomycosis of the toenail due to *Trichophyton* that has been confirmed by a fungal diagnostic test.

RATIONALE
These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Onmel is indicated for the treatment of onychomycosis of the toenail due to *Trichophyton rubrum* or *T. mentagrophytes* in non-immunocompromised patients. Prior to initiating treatment, appropriate nail specimens for laboratory testing potassium hydroxide (KOH preparation, fungal culture, or nail biopsy) should be obtained to confirm the diagnosis of onychomycosis. The recommended dose of Onmel is 200 mg once daily for 12 consecutive weeks.

REFERENCES

Written by: UM Development (CT)
Date Written: 01/2013
Revised: (PL) 08/2013, 08/2014; (MS) 05/2015, 05/2016 (no clinical changes), (SE) 06/2016 (created separate Med D); (MS) 04/2017; (DS) 04/2018 (no clinical changes), (ME) 02/2019 (no clinical changes)
Reviewed: Medical Affairs: (DNC) 01/2013; (DNC) 08/2013; (LCB) 08/2014; (LS) 05/2015; (AN) 04/2017; (DNC) 04/2018
External Review: 01/2013, 02/2013, 12/2013, 10/2014, 10/2015, 08/2016, 08/2017, 06/2018, 06/2019

Itraconazole (Onmel Tablets) MDC-1 919-A 02-2019 ©2019 CVS Caremark. All rights reserved.

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**CRITERIA FOR APPROVAL**

1. Is the requested drug being prescribed for the treatment of onychomycosis of the toenail due to *Trichophyton* that has been confirmed by a fungal diagnostic test?  
   - Yes  
   - No

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<th>DENIAL REASONS – DO NOT USE FOR MEDICARE PART D</th>
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| Yes 1. Approve, 3 months | Deny  
You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions:  
- You have a specific fungal infection of the toenail  
- You had a test to confirm your toenail fungus  
Your request has been denied based on the information we have.  
[Short Description: No approvable diagnosis, no confirmation of diagnosis]  

PRIOR AUTHORIZATION CRITERIA

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<th>BRAND NAME* (generic)</th>
<th>SPORANOX ORAL CAPSULES (itraconazole)</th>
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* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Sporanox (itraconazole) Capsules are indicated for the treatment of the following fungal infections in immunocompromised and non-immunocompromised patients:

1. Blastomycosis, pulmonary and extrapulmonary
2. Histoplasmosis, including chronic cavitary pulmonary disease and disseminated, non-meningeal histoplasmosis, and
3. Aspergillosis, pulmonary and extrapulmonary, in patients who are intolerant of or who are refractory to amphotericin B therapy.

Specimens for fungal cultures and other relevant laboratory studies (wet mount, histopathology, serology) should be obtained before therapy to isolate and identify causative organisms. Therapy may be instituted before the results of the cultures and other laboratory studies are known; however, once these results become available, antifungal therapy should be adjusted accordingly.

Sporanox Capsules are also indicated for the treatment of the following fungal infections in non-immunocompromised patients:

1. Onychomycosis of the toenail, with or without fingernail involvement, due to dermatophytes (tinea unguium), and
2. Onychomycosis of the fingernail due to dermatophytes (tinea unguium).

Prior to initiating treatment, appropriate nail specimens for laboratory testing (KOH preparation, fungal culture, or nail biopsy) should be obtained to confirm the diagnosis of onychomycosis.

Compendial Uses

- Coccidioidomycosis
- Cryptococcosis
- Microsporidiosis
- Penicilliosis
- Pityriasis versicolor/Tinea versicolor
- Sporotrichosis
- Tinea corporis, Tinea cruris, Tinea capitis, Tinea manuum, Tinea pedis

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- Patient has one of the following diagnoses: A) Pityriasis versicolor, B) Tinea versicolor, C) Onychomycosis due to tinea that has been confirmed by a fungal diagnostic test

  OR

- Patient has one of the following diagnoses: A) Blastomycosis, B) Histoplasmosis, C) Aspergillosis, D) Coccidioidomycosis, E) Cryptococcosis, F) Sporotrichosis, G) Penicilliosis, H) Microsporidiosis

  OR

- Patient has one of the following diagnoses: A) Tinea corporis, B) Tinea cruris, C) Tinea capitis, D) Tinea manuum, E) Tinea pedis

  AND

  - Patient experienced an inadequate treatment response, adverse event, intolerance, or contraindication to griseofulvin
RATIONALE
These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. The criteria do not provide treatment for cosmetic purposes. Sporanox (itraconazole) capsules are indicated for the treatment of blastomycosis, pulmonary and extrapulmonary; histoplasmosis, including chronic cavitary pulmonary disease and disseminated, non-meningeal histoplasmosis, and; aspergillosis, pulmonary and extrapulmonary, in patients who are intolerant of or who are refractory to amphotericin B therapy. Specimens for fungal cultures and other relevant laboratory studies (wet mount, histopathology, serology) should be obtained before therapy to isolate and identify causative organisms. Therapy may be instituted before the results of the cultures and other laboratory studies are known; however, once these results become available, anti-infective therapy should be adjusted accordingly. Acceptable compendia also indicate that itraconazole is appropriate for the treatment of coccidioidomycosis, cryptococcosis, sporotrichosis, penicilliosis, and microsporidiosis. Sporanox capsules are also indicated in non-immunocompromised patients for the treatment of onychomycosis of the toenail, with or without fingernail involvement, due to dermatophytes (tinea unguium); and onychomycosis of the fingernail due to dermatophytes (tinea unguium). Prior to initiating treatment, appropriate nail specimens for laboratory testing potassium hydroxide (KOH) preparation, fungal culture, or nail biopsy should be obtained to confirm the diagnosis of onychomycosis. Per the compendia, itraconazole is suggested as an alternative therapy for the treatment of pityriasis versicolor, tinea versicolor, tinea corporis, tinea cruris, tinea capitis, tinea manuum or tinea pedis.

Itraconazole will be approved for the treatment of onychomycosis due to dermatophytes (tinea unguium) following confirmation with a fungal diagnostic test (e.g., KOH preparation, fungal culture, or nail biopsy). Itraconazole will be approved for the treatment of patients with either pityriasis versicolor or tinea versicolor. Itraconazole will be approved for the treatment of tinea corporis, tinea cruris, tinea capitis, tinea manuum or tinea pedis following a trial of griseofulvin as it is FDA approved as first line therapy. Itraconazole will be approved for the treatment of blastomycosis, histoplasmosis, aspergillosis, coccidioidomycosis, cryptococcosis, sporotrichosis, penicilliosis, and microsporidiosis.

The recommended treatment course for onychomycosis of the toenails, with or without fingernail involvement, is 200 mg once daily for 12 weeks. The suggested dosing for superficial tinea infections is similar to that of onychomycosis of the toenails, 200 mg once daily, although for a shorter duration. Therefore, coverage for these conditions will be approved for up to 3 months. The recommended and suggested treatments for the remainder of the approvable indications vary depending on the type of infection and patient specific factors. It is noted, however, that treatment in life-threatening situations should be continued for a minimum of 3 months and until clinical parameters and laboratory tests indicate that the active fungal infection has subsided. An inadequate period of treatment may lead to recurrence of active infection. Because of this, the duration of approval for these indications will be set at 6 months.

REFERENCES

**CRITERIA FOR APPROVAL**

1. Does the patient have one of the following diagnoses: A) Pityriasis versicolor, B) Tinea versicolor, C) Onychomycosis due to tinea that has been confirmed by a fungal diagnostic test? [If yes, then no further questions.]
   - Yes
   - No

2. Does the patient have any of the following diagnoses: A) Tinea corporis, B) Tinea cruris, C) Tinea capitis, D) Tinea manuum, E) Tinea pedis? [If no, then skip to question 4.]
   - Yes
   - No

3. Has the patient experienced an inadequate treatment response, intolerance or contraindication to griseofulvin? [No further questions.]
   - Yes
   - No

4. Does the patient have one of the following diagnoses: A) Blastomycosis, B) Histoplasmosis, C) Aspergillosis, D) Coccidioidomycosis, E) Cryptococcosis, F) Sporotrichosis, G) Penicilliosis, H) Microsporidiosis?
   - Yes
   - No

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<th>Duration of Approval</th>
<th>3 Months</th>
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**Duration of Approval**

- **Set 3**
  - Yes to question(s) No to question(s)
  - 4 1

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<thead>
<tr>
<th>Mapping Instructions</th>
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<tr>
<td>1. Approve, 3 months</td>
<td>Go to 2</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have these conditions: - You had a poor response to griseofulvin or cannot take it. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis, no inadequate response, intolerance or contraindication to griseofulvin]</td>
<td></td>
</tr>
<tr>
<td>2. Go to 3</td>
<td>Go to 4</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have one of these conditions: - You have ringworm, a fungal infection of the groin, scalp, or hand, or athlete’s foot - You have a specific fungal infection of the skin that causes spots - You have a specific nail fungus and it has been tested - You have Blastomycosis, Histoplasmosis, Aspergillosis, Coccidioidomycosis, Cryptococciosis, Sporotrichosis, Penicilliosis or Microsporidiosis Your request has been denied based on the information we have. [Short Description: No approvable diagnosis, no confirmation of diagnosis]</td>
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</table>
PRIOR AUTHORIZATION CRITERIA

BRAND NAME* (generic) SPORANOX ORAL SOLUTION (itraconazole)

Status: CVS Caremark Criteria Type: Initial Prior Authorization Ref # 1286-A

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS
Sporanox (itraconazole) Oral Solution is indicated for the treatment of oropharyngeal and esophageal candidiasis.

COMPENDIAL USES
Blastomycosis3,4
Histoplasmosis3,4
Aspergillosis3,4
Coccidioidomycosis3,4
Cryptococcosis3,4
Microsporidiosis3
Penicilliosis3
Pityriasis versicolor/Tinea versicolor4
Sporotrichosis3,4
Tinea corporis, Tinea cruris, Tinea capitis, Tinea manuum, Tinea pedis4

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- Patient has a diagnosis of oropharyngeal candidiasis or esophageal candidiasis.

  OR

- Patient is unable to take itraconazole capsules due to one of the following: inability to swallow itraconazole capsules or inability to achieve therapeutic levels with itraconazole capsules.

  AND

- Patient has one of the following diagnoses: A) Pityriasis versicolor, B) Tinea versicolor, C) Onychomycosis due to tinea that has been confirmed by a fungal diagnostic test

  OR

- Patient has one of the following diagnoses: A) Blastomycosis, B) Histoplasmosis, C) Aspergillosis, D) Coccidioidomycosis, E) Cryptococcosis, F) Sporotrichosis, G) Penicilliosis, H) Microsporidiosis

  OR

- Patient has one of the following diagnoses: A) Tinea corporis, B) Tinea cruris, C) Tinea capitis, D) Tinea manuum, E) Tinea pedis.

  AND

  o Patient experienced an inadequate treatment response, adverse event, intolerance, or contraindication to griseofulvin

RATIONALE
The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Sporanox (itraconazole) Oral Solution is indicated for the treatment of oropharyngeal and esophageal candidiasis.
For oropharyngeal candidiasis, Sporanox (itraconazole) Oral Solution should be taken for 1 to 2 weeks. For patients with oropharyngeal candidiasis unresponsive/refractory to treatment with fluconazole tablets responding to Sporanox (itraconazole) Oral Solution therapy, clinical response will be seen in 2 to 4 weeks. Patients may be expected to relapse shortly after discontinuing therapy. There is limited data on the safety of long-term use, greater than 6 months, of Sporanox (itraconazole) Oral Solution. For esophageal candidiasis, Sporanox (itraconazole) Oral Solution should be taken for a minimum treatment of 3 weeks. Treatment should continue for 2 weeks following resolution of symptoms. Sporanox (itraconazole) Oral Solution and Sporanox (itraconazole) Capsules should not be used interchangeably as only Sporanox (itraconazole) Oral Solution has been demonstrated effective for oral and/or esophageal candidiasis.1-4

Although it is not recommend to use Sporanox (itraconazole) capsules interchangeably with Sporanox (itraconazole) Oral Solution for the treatment or oral and/or esophageal candidiasis, it is reasonable to assume that the interchange can work in the opposite direction. That is to say, Sporanox (itraconazole) Oral Solution can be approved for the same indications/compendia uses as Sporanox (itraconazole) capsules. For these uses, the patient must be unable to take the capsules (due to an inability to swallow or achieve therapeutic levels with itraconazole capsules). The criteria do not provide treatment for cosmetic purposes. Itraconazole can be used for the treatment of blastomycosis, pulmonary and extrapulmonary; histoplasmosis, including chronic cavitary pulmonary disease and disseminated, non-meningeal histoplasmosis, and; aspergillosis, pulmonary and extrapulmonary, in patients who are intolerant of or who are refractory to amphotericin B therapy.2,4 Specimens for fungal cultures and other relevant laboratory studies (wet mount, histopathology, serology) should be obtained before therapy to isolate and identify causative organisms. Therapy may be instituted before the results of the cultures and other laboratory studies are known; however, once these results become available, anti-infective therapy should be adjusted accordingly. Acceptable compendia also show that itraconazole is appropriate for the treatment of coccidioidomycosis, cryptococcosis, sporotrichosis, penicilliosis, and microsporidiosis. Itraconazole can also be used in non-immunocompromised patients for the treatment of onychomycosis of the toenail, with or without fingernail involvement, due to dermatophytes (tinea unguium); and onychomycosis of the fingernail due to dermatophytes (tinea unguium).3,4,9,10 Prior to initiating treatment, appropriate nail specimens for laboratory testing potassium hydroxide (KOH) preparation, fungal culture, or nail biopsy should be obtained to confirm the diagnosis of onychomycosis. Per the compendia, itraconazole is suggested as an alternative therapy for the treatment of pityriasis versicolor or tinea versicolor, tinea corporis, tinea cruris, tinea capitis, tinea manuum or tinea pedis.3,4

Itraconazole will be approved for the treatment of onychomycosis due to dermatophytes (tinea unguium) following confirmation with a fungal diagnostic test (e.g., KOH preparation, fungal culture, or nail biopsy). Itraconazole will be approved for the treatment of patients with either pityriasis versicolor or tinea versicolor. Itraconazole will be approved for the treatment of tinea corporis, tinea cruris, tinea capitis, tinea manuum or tinea pedis following a trial of griseofulvin as it is FDA approved as first line therapy. Itraconazole will be approved for the treatment of blastomycosis, histoplasmosis, aspergillosis, coccidioidomycosis, cryptococcosis, sporotrichosis, penicilliosis, and microsporidiosis.

The recommended treatment course for onychomycosis of the toenails, with or without fingernail involvement, is 200 mg once daily for 12 weeks.2 The suggested dosing for superficial tinea infections is similar to that of onychomycosis of the toenails, 200 mg once daily, although for a shorter duration.4 Therefore, coverage for these conditions will be approved for up to 3 months. The recommended and suggested treatments for the remainder of the approvable indications vary depending on the type of infection and patient specific factors. It is noted, however, that treatment in life-threatening situations should be continued for a minimum of 3 months and until clinical parameters and laboratory tests indicate that the active fungal infection has subsided. An inadequate period of treatment may lead to recurrence of active infection.2 Because of this, the duration of approval for these indications will be set at 6 months.

REFERENCES


**CRITERIA FOR APPROVAL**

<table>
<thead>
<tr>
<th></th>
<th>Does the patient have any of the following diagnoses: A) Oropharyngeal candidiasis, B) Esophageal candidiasis? [If yes, then no further questions.]</th>
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<th>Is the patient unable to take itraconazole capsules due to one of the following: A) inability to swallow itraconazole capsules, B) inability to achieve therapeutic levels with itraconazole capsules?</th>
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<th>Does the patient have one of the following diagnoses: A) Tinea corporis, B) Tinea cruris, C) Tinea capitis, D) Tinea manuum, E) Tinea pedis? [If no, then skip to question 6.]</th>
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<th>Has the patient experienced an inadequate treatment response, intolerance or contraindication to griseofulvin? [No further questions.]</th>
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<th>Does the patient have one of the following diagnoses: A) Blastomycosis, B) Histoplasmosis, C) Aspergillosis, D) Coccioidiomycosis, E) Cryptococcosis, F) Sporotrichosis, G) Penicilliosis, H) Microsporidiosis?</th>
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<tr>
<td>1.</td>
<td>Approve, 6 months</td>
<td>Go to 2</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions: - You have a fungal infection of the mouth or throat (Oropharyngeal candidiasis or Esophageal candidiasis) - You are unable to swallow capsules - You are unable to get a strong enough dose with capsules Your request has been denied based on the information we have. [Short Description: No approvable diagnosis, no justification for solution over capsules]</td>
</tr>
<tr>
<td>2.</td>
<td>Go to 3</td>
<td>Deny</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions: - You have a fungal infection of the mouth or throat (Oropharyngeal candidiasis or Esophageal candidiasis) - You are unable to swallow capsules - You are unable to get a strong enough dose with capsules Your request has been denied based on the information we have. [Short Description: No approvable diagnosis, no justification for solution over capsules]</td>
</tr>
<tr>
<td>3.</td>
<td>Approve, 3 months</td>
<td>Go to 4</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have these conditions: - You had a poor response to griseofulvin or cannot take it Your request has been denied based on the information we have. [Short Description: No approvable diagnosis, no inadequate response, intolerance or contraindication to griseofulvin]</td>
</tr>
<tr>
<td>4.</td>
<td>Go to 5</td>
<td>Go to 6</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have one of these conditions: - You have ringworm, a fungal infection of the groin, scalp or hand, or athlete’s foot - You have a specific fungal infection of the skin that causes spots - You have a specific nail fungus and it has been tested - You have Blastomycosis, Histoplasmosis, Aspergillosis, Coccidioidomycosis, Cryptococcosis, Sporotrichosis, Penicilliosis or Microsporidiosis Your request has been denied based on the information we have. [Short Description: No approvable diagnosis, no confirmation of diagnosis]</td>
</tr>
<tr>
<td>5.</td>
<td>Approve, 3 months</td>
<td>Deny</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have one of these conditions: - You have ringworm, a fungal infection of the groin, scalp or hand, or athlete’s foot - You have a specific fungal infection of the skin that causes spots - You have a specific nail fungus and it has been tested - You have Blastomycosis, Histoplasmosis, Aspergillosis, Coccidioidomycosis, Cryptococcosis, Sporotrichosis, Penicilliosis or Microsporidiosis Your request has been denied based on the information we have. [Short Description: No approvable diagnosis, no confirmation of diagnosis]</td>
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<td>6.</td>
<td>Approve, 6 months</td>
<td>Deny</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have one of these conditions: - You have ringworm, a fungal infection of the groin, scalp or hand, or athlete’s foot - You have a specific fungal infection of the skin that causes spots - You have a specific nail fungus and it has been tested - You have Blastomycosis, Histoplasmosis, Aspergillosis, Coccidioidomycosis, Cryptococcosis, Sporotrichosis, Penicilliosis or Microsporidiosis Your request has been denied based on the information we have. [Short Description: No approvable diagnosis, no confirmation of diagnosis]</td>
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# PRIOR AUTHORIZATION CRITERIA

**BRAND NAME***
(generic)

**TOLSURA**
(itraconazole)

**Status:** CVS Caremark Criteria  
**Type:** Initial Prior Authorization  
**Ref # 2845-A**

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

## FDA-APPROVED INDICATIONS
TOLSURA is an azole antifungal indicated for the treatment of the following fungal infections in immunocompromised and non-immunocompromised adult patients:

1. Blastomycosis, pulmonary and extrapulmonary
2. Histoplasmosis, including chronic cavitary pulmonary disease and disseminated, non-meningeal histoplasmosis, and  
3. Aspergillosis, pulmonary and extrapulmonary, in patients who are intolerant of or who are refractory to amphotericin B therapy.

Specimens for fungal cultures and other relevant laboratory studies (wet mount, histopathology, serology) should be obtained before therapy to isolate and identify causative organisms. Therapy may be instituted before the results of the cultures and other laboratory studies are known; however, once these results become available, anti-fungal therapy should be adjusted accordingly.

Limitations of Use:
TOLSURA is not indicated for the treatment of onychomycosis  
TOLSURA is NOT interchangeable or substitutable with other itraconazole products

## COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has one of the following diagnoses: A) Blastomycosis, B) Histoplasmosis, C) Aspergillosis

## RATIONALE
The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. The criteria do not provide treatment for cosmetic purposes. Tolsura is indicated for the treatment of blastomycosis, pulmonary and extrapulmonary; histoplasmosis, including chronic cavitary pulmonary disease and disseminated, non-meningeal histoplasmosis, and aspergillosis, pulmonary and extrapulmonary, in patients who are intolerant of or who are refractory to amphotericin B therapy. Specimens for fungal cultures and other relevant laboratory studies (wet mount, histopathology, serology) should be obtained before therapy to isolate and identify causative organisms. Therapy may be instituted before the results of the cultures and other laboratory studies are known; however, once these results become available, anti-infective therapy should be adjusted accordingly.

Tolsura will be approved for the treatment of blastomycosis, histoplasmosis, aspergillosis. Treatment in life-threatening situations should be continued for a minimum of 3 months and until clinical parameters and laboratory tests indicate that the active fungal infection has subsided. An inadequate period of treatment may lead to recurrence of active infection. Therefore, the duration of approval for these indications will be set at 6 months.

## REFERENCES
2. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA.  
CRITERIA FOR APPROVAL

1. Does the patient have one of the following diagnoses: A) Blastomycosis, B) Histoplasmosis, C) Aspergillosis?

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**Mapping Instructions**

- **DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
  - You do not meet the requirements of your plan.
  - Your plan covers this drug when you have Blastomycosis, Histoplasmosis or Aspergillosis.
  - Your request has been denied based on the information we have.
  - [Short Description: No approvable diagnosis]
SPECIALTY GUIDELINE MANAGEMENT

Intravenous Immune Globulin (IVIG):
Asceniv™, Bivigam®, Carimune® NF, Flebogamma® DIF, Gammagard® Liquid, Gammagard® S/D, Gammaked™, Gammaplex®, Gamunex®-C, Octagam®, Panzyga®, and Privigen®

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Primary immunodeficiency
2. Idiopathic thrombocytopenic purpura (ITP)
3. Chronic inflammatory demyelinating polyneuropathy
4. Multifocal motor neuropathy
5. Kawasaki syndrome
6. B-cell chronic lymphocytic leukemia (CLL)

B. Compendial Uses
1. Prophylaxis of bacterial infections in pediatric human immunodeficiency virus (HIV) infection
2. Prophylaxis of bacterial infections in bone marrow transplant (BMT)/hematopoietic stem cell transplant (HSCT) recipients
3. Dermatomyositis
4. Polymyositis
5. Myasthenia gravis
6. Guillain-Barré syndrome
7. Lambert-Eaton myasthenic syndrome
8. Fetal/neonatal alloimmune thrombocytopenia
9. Parvovirus B19-induced pure red cell aplasia
10. Stiff-person syndrome
11. Management of immune checkpoint inhibitor-related nervous system adverse events

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review:

A. Primary immunodeficiency
1. Diagnostic test results (when applicable)
   a. Copy of laboratory report with serum immunoglobulin levels: IgG, IgA, IgM, and IgG subclasses
   b. Vaccine response to pneumococcal polysaccharide vaccine (post-vaccination Streptococcus pneumoniae antibody titers)
   c. Pertinent genetic or molecular testing in members with a known genetic disorder
   d. Copy of laboratory report with lymphocyte subset enumeration by flow cytometry
2. IgG trough level for those continuing with IVIG therapy

B. Secondary hypogammaglobulinemia (CLL, HIV, BMT/HSCT recipients)
   1. Copy of laboratory report with pre-treatment serum IgG level (when applicable)

C. Chronic inflammatory demyelinating polyneuropathy (CIDP) and multifocal motor neuropathy (MMN)
   1. Pre-treatment electodiagnostic studies (electromyography [EMG] or nerve conduction studies [NCS])
   2. For CIDP, pre-treatment cerebrospinal fluid (CSF) analysis (when available)

D. Dermatomyositis and polymyositis
   1. Pre-treatment electodiagnostic studies (EMG/NCS)
   2. Pre-treatment muscle biopsy report (when available)

E. Lambert-Eaton Myasthenic Syndrome (LEMS)
   1. Neurophysiology studies (e.g., electromyography) (when applicable)
   2. A positive anti-P/Q type voltage-gated calcium channel antibody test (when applicable)

III. CRITERIA FOR INITIAL APPROVAL

A. Primary Immunodeficiency
   Initial authorization of 12 months may be granted for members with any of the following diagnoses:
   1. Severe combined immunodeficiency (SCID) or congenital agammaglobulinemia (e.g., X-linked or autosomal recessive agammaglobulinemia):
      a. Diagnosis confirmed by genetic or molecular testing, or
      b. Pretreatment IgG level < 200 mg/dL, or
      c. Absence or very low number of T cells (CD3 T cells < 300/microliter) or the presence of maternal T cells in the circulation (SCID only)
   2. Wiskott-Aldrich syndrome, DiGeorge syndrome, or ataxia-telangiectasia (or other non-SCID combined immunodeficiency):
      a. Diagnosis confirmed by genetic or molecular testing (if applicable), and
      b. History of recurrent bacterial infections (e.g., pneumonia, otitis media, sinusitis, sepsis, gastrointestinal), and
      c. Impaired antibody response to pneumococcal polysaccharide vaccine (see Appendix A)
   3. Common variable immunodeficiency (CVID):
      a. Age 4 years or older
      b. Other causes of immune deficiency have been excluded (e.g., drug induced, genetic disorders, infectious diseases such as HIV, malignancy)
      c. Pretreatment IgG level < 500 mg/dL or ≥ 2 SD below the mean for age
      d. History of recurrent bacterial infections
      e. Impaired antibody response to pneumococcal polysaccharide vaccine (see Appendix A)
   4. Hypogammaglobulinemia (unspecified), IgG subclass deficiency, selective IgA deficiency, selective IgM deficiency, or specific antibody deficiency:
      a. History of recurrent bacterial infections
      b. Impaired antibody response to pneumococcal polysaccharide vaccine (see Appendix A)
      c. Any of the following pre-treatment laboratory findings:
         i. Hypogammaglobulinemia: IgG < 500 mg/dL or ≥ 2 SD below the mean for age
         ii. Selective IgA deficiency: IgA level < 7 mg/dL with normal IgG and IgM levels
         iii. Selective IgM deficiency: IgM level < 30 mg/dL with normal IgG and IgA levels
         iv. IgG subclass deficiency: IgG1, IgG2, or IgG3 ≥ 2 SD below mean for age assessed on at least 2 occasions; normal IgG (total) and IgM levels, normal/low IgA levels
         v. Specific antibody deficiency: normal IgG, IgA and IgM levels
   5. Other predominant antibody deficiency disorders must meet a., b., and c.i. in section 4. above.
   6. Other combined immunodeficiency must meet criteria in section 2. above.
Re-authorization of 24 months may be granted when the following criteria are met:
1. A reduction in the frequency of bacterial infections has been demonstrated since initiation of IVIG therapy, AND
2. IgG trough levels are monitored at least yearly and maintained at or above the lower range of normal for age (when applicable for indication), OR
3. The prescriber will re-evaluate the dose of IVIG and consider a dose adjustment (when appropriate).

Gammagard Liquid, Gamunex-C, and Gammaked may be administered intravenously or subcutaneously for primary immunodeficiency.

B. Myasthenia Gravis
1. Authorization of 1 month may be granted to members who are prescribed IVIG for worsening weakness, acute exacerbation, or in preparation for surgery.
   a. Worsening weakness includes an increase in any of the following symptoms: diplopia, ptosis, blurred vision, difficulty speaking (dysarthria), difficulty swallowing (dysphagia), difficulty chewing, impaired respiratory status, fatigue, and limb weakness. Acute exacerbations include more severe swallowing difficulties and/or respiratory failure
   b. Pre-operative management (eg, prior to thymectomy)
2. Authorization of 12 months may be granted to members with refractory myasthenia gravis who have tried and failed 2 or more of standard therapies (eg, corticosteroids, azathioprine, cyclosporine, mycophenolate mofetil, rituximab).

C. Chronic Inflammatory Demyelinating Polineuropathy (CIDP)
1. Initial authorization of 3 months may be granted when the following criteria are met:
   a. Moderate to severe functional disability
   b. The diagnosis was confirmed by electrodiagnostic studies and the evaluation of cerebrospinal fluid (CSF)
2. Re-authorization of 24 months may be granted when the following criteria are met:
   a. Significant improvement in disability and maintenance of improvement since initiation of IVIG therapy
   b. IVIG is being used at the lowest effective dose and frequency

D. Dermatomyositis or Polymyositis
1. Initial authorization of 3 months may be granted when the following criteria are met:
   a. Diagnosis established by clinical features (eg, proximal weakness, rash), elevated muscle enzyme levels, electrodiagnostic studies, and muscle biopsy (when available); supportive diagnostic tests include autoantibody testing and muscle imaging (eg, MRI), and
   b. Standard first-line treatments (corticosteroids or immunosuppressants) have been tried but were unsuccessful or not tolerated, or
   c. Member is unable to receive standard first-line therapy because of a contraindication or other clinical reason.
2. Re-authorization of 12 months may be granted when the following criterion is met:
   a. Significant improvement in disability and maintenance of improvement since initiation of IVIG therapy

E. Idiopathic Thrombocytopenic Purpura (Immune Thrombocytopenia)
1. Newly diagnosed ITP (diagnosed within the past 3 months) or initial therapy: authorization of 1 month may be granted when the following criteria are met:
   a. Children (< 18 years of age)
      i. Significant bleeding symptoms (mucosal bleeding or other moderate/severe bleeding) or
      ii. High risk for bleeding* (see Appendix B), or
iii. Rapid increase in platelets is required* (eg, surgery or procedure)
b. Adults (≥ 18 years of age)
i. Platelet count < 30,000/mcL, or
ii. Platelet count < 50,000/mcL and significant bleeding symptoms, high risk for bleeding or rapid increase in platelets is required*, and
iii. Corticosteroid therapy is contraindicated and IVIG will be used alone or IVIG will be used in combination with corticosteroid therapy

2. Chronic/persistent ITP (≥ 3 months from diagnosis) or ITP unresponsive to first-line therapy: authorization of 6 months may be granted when the following criteria are met:
a. Platelet count < 30,000/mcL, or
b. Platelet count < 50,000/mcL and significant bleeding symptoms, high risk for bleeding* or rapid increase in platelets is required*, and
c. Relapse after previous response to IVIG or inadequate response/intolerance/contraindication to corticosteroid or anti-D therapy

3. Adults with refractory ITP after splenectomy: authorization of 6 months may be granted when either of the following criteria is met:
a. Platelet count < 30,000/mcL, or
b. Significant bleeding symptoms

4. ITP in pregnant women: authorization through delivery may be granted to pregnant women with ITP.

* The member’s risk factor(s) for bleeding (see Appendix B) or reason requiring a rapid increase in platelets must be provided.

F. B-cell Chronic Lymphocytic Leukemia (CLL)
1. Initial authorization of 6 months may be granted when the following criteria are met:
a. IVIG is prescribed for prophylaxis of bacterial infections.
b. Member has a history of recurrent sinopulmonary infections requiring intravenous antibiotics or hospitalization.
c. Member has a pretreatment serum IgG level <500 mg/dL.

2. Re-authorization of 6 months may be granted when a reduction in the frequency of bacterial infections has been demonstrated since initiation of IVIG therapy.

G. Prophylaxis of Bacterial Infections in HIV-Infected Pediatric Patients
1. Initial authorization of 6 months may be granted to pediatric members with HIV infection when the following criteria are met:
a. Member is ≤ 12 years of age.
b. IVIG is prescribed for primary prophylaxis of bacterial infections and pretreatment serum IgG < 400 mg/dL, or
c. IVIG is prescribed for secondary prophylaxis of bacterial infections for members with a history of recurrent bacterial infections (> 2 serious bacterial infections in a 1-year period)

2. Re-authorization of 6 months may be granted when a reduction in the frequency of bacterial infections has been demonstrated since initiation of IVIG therapy.

H. Prophylaxis of Bacterial Infections in BMT/HSCT Recipients
1. Initial authorization of 6 months may be granted to members who are BMT/HSCT recipients when the following criteria are met:
a. IVIG is prescribed for prophylaxis of bacterial infections.
b. Either of the following:
   i. IVIG is requested within the first 100 days post-transplant.
   ii. Member has a pretreatment serum IgG < 400 mg/dL.

2. Re-authorization of 6 months may be granted when a reduction in the frequency of bacterial infections has been demonstrated since initiation of IVIG therapy.
I. Multifocal Motor Neuropathy (MMN)
   1. Initial authorization of 3 months may be granted when the following criteria are met:
      a. Weakness without objective sensory loss in 2 or more nerves
      b. The diagnosis was confirmed by electrodiagnostic studies
   2. Re-authorization of 24 months may be granted when significant improvement in disability and
      maintenance of improvement have occurred since initiation of IVIG therapy

J. Guillain-Barre Syndrome (GBS)
   Authorization of 2 months total may be granted for the treatment of GBS.

K. Lambert-Eaton Myasthenic Syndrome (LEMS)
   Authorization of 6 months may be granted for LEMS when the diagnosis has been confirmed by either of
   the following:
   1. Neurophysiology studies (e.g., electromyography)
   2. A positive anti- P/Q type voltage-gated calcium channel antibody test

L. Kawasaki Syndrome
   Authorization of 1 month may be granted for pediatric members with Kawasaki syndrome.

M. Fetal/Neonatal Alloimmune Thrombocytopenia (F/NAIT)
   Authorization of 6 months may be granted for treatment of F/NAIT.

N. Parvovirus B19-induced Pure Red Cell Aplasia (PRCA)
   Authorization of 6 months may be granted for parvovirus B19-induced PRCA.

O. Stiff-person Syndrome
   Authorization of 6 months may be granted for treatment of stiff-person syndrome.

P. Management of immune checkpoint inhibitor-related nervous system adverse events
   Authorization of 1 month may be granted for management of immune checkpoint-inhibitor toxicities when
   all of the following criteria are met:
   1. Member has experienced a moderate or severe adverse event to a PD-1 or PD-L1 inhibitor (eg,
      pembrolizumab, nivolumab, atezolizumab, avelumab, durvalumab)
   2. The offending medication has been held or discontinued
   3. Member experienced one or more of the following nervous system adverse events: pneumonitis,
      myasthenia gravis, peripheral neuropathy, encephalitis or transverse myelitis

IV. CONTINUATION OF THERAPY
   Authorization may be granted for continuation of therapy when either the following criteria is met:
   A. For conditions with reauthorization criteria listed under section III: Members who are currently
      receiving IVIG therapy must meet the applicable reauthorization criteria for the member's condition.
   B. For all other conditions, all members (including new members) must meet initial authorization criteria.

V. OTHER
   When Gammagard Liquid, Gamunex-C and Gammaked will be administered subcutaneously, they may be
   approved for primary immunodeficiency only.
VI. APPENDICES

Appendix A: Impaired Antibody Response to Pneumococcal Polysaccharide Vaccine
- Age 2 years and older: impaired antibody response demonstrated to vaccination with a pneumococcal polysaccharide vaccine
- Not established for children less than 2 years of age
- Excludes the therapy initiated in the hospital setting

Appendix B: Examples of Risk Factors for Bleeding (not all inclusive)
- Undergoing a medical or dental procedure where blood loss is anticipated
- Comorbidity (eg, peptic ulcer disease, hypertension)
- Mandated anticoagulation therapy
- Profession or lifestyle predisposes patient to trauma (eg, construction worker, fireman, professional athlete)

VII. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

IXEMPRA (ixabepilone)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. In combination with capecitabine for the treatment of metastatic or locally advanced breast cancer resistant to treatment with an anthracycline and a taxane, or whose cancer is taxane resistant and for whom further anthracycline therapy is contraindicated
   2. Monotherapy for the treatment of metastatic or locally advanced breast cancer in patients whose tumors are resistant or refractory to anthracyclines, taxanes, and capecitabine

B. Compendial Uses
   1. Human epidermal growth factor receptor 2 (HER2)-negative recurrent or stage IV (M1) breast cancer
   2. HER2-positive recurrent or stage IV (M1) breast cancer in combination with trastuzumab

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Breast Cancer
Authorization of 12 months may be granted for the treatment of breast cancer.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

JAKAFI (ruxolitinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Jakafi is indicated for treatment of patients with intermediate or high-risk myelofibrosis, including primary myelofibrosis, post-polycythemia vera myelofibrosis and post-essential thrombocytopenia myelofibrosis.
   2. Jakafi is indicated for treatment of patients with polycythemia vera who have had an inadequate response to or are intolerant of hydroxyurea.

B. Compendial Uses
   1. Symptomatic low-risk or intermediate-risk 1 myelofibrosis
   2. Accelerated phase or blast phase myelofibrosis
   3. Polycythemia vera in patients with inadequate response or loss of response to interferon therapy
   4. Steroid-refractory acute or chronic graft versus host-disease (GVHD)
   5. B-cell Acute Lymphoblastic (Lymphocytic) Leukemia (ALL)

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Myelofibrosis
   Authorization of 12 months may be granted for the treatment of myelofibrosis.

B. Polycythemia Vera
   Authorization of 12 months may be granted for the treatment of polycythemia vera to members who have had an inadequate response or intolerance to hydroxyurea or interferon therapy (ie, interferon alfa-2b, peginterferon alfa-2a, or peginterferon alfa-2b).

C. Steroid-refractory acute or chronic graft versus host-disease (GVHD)
   Authorization of 12 months may be granted for the treatment of steroid-refractory acute or chronic graft versus host-disease (GVHD).

D. B-cell Acute Lymphoblastic (Lymphocytic) Leukemia (ALL)
   Authorization of 12 months may be granted for the treatment of B-cell Acute Lymphoblastic (Lymphocytic) Leukemia for members with either a cytokine receptor-like factor 2 (CRLF2) mutation or a Janus kinase (JAK) mutation.

III. CONTINUATION OF THERAPY
All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

JEVTANA (cabazitaxel)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Jevtana is indicated in combination with prednisone for the treatment of patients with hormone-refractory metastatic prostate cancer previously treated with a docetaxel-containing treatment regimen.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 24 months may be granted for the treatment of metastatic prostate cancer.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

PRIOR AUTHORIZATION CRITERIA

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* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS
Jublia (efinaconazole) topical solution, 10% is an azole antifungal indicated for the topical treatment of onychomycosis of the toenail(s) due to Trichophyton rubrum and Trichophyton mentagrophytes.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for onychomycosis of the toenail(s) due to Trichophyton rubrum or Trichophyton mentagrophytes, which has been confirmed with a fungal diagnostic test (e.g., potassium hydroxide [KOH] preparation, fungal culture, or nail biopsy) AND
- The patient has experienced an inadequate treatment response, intolerance, or contraindication to an oral antifungal therapy (e.g., terbinafine, itraconazole)

RATIONALE
These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Jublia (efinaconazole) topical solution, 10% is an azole antifungal indicated for the topical treatment of onychomycosis of the toenail(s) due to Trichophyton rubrum and Trichophyton mentagrophytes. Jublia is to be applied to affected toenails once daily for 48 weeks, using the integrated flow-through brush applicator. When applying Jublia, the toenail, the toenail folds, toenail bed, hyponychium, and the undersurface of the toenail plate are to be completely covered.

Accurate diagnosis of onychomycosis involves physical and microscopic examination and culture. Only 50% of nail problems are caused by onychomycosis, and clinical diagnosis by physical examination alone can be inaccurate. When onychomycosis is suspected, samples should be taken to conduct diagnostic tests. Samples are then prepared with potassium hydroxide (KOH) solution to be viewed under a microscope to look for the presence of a fungal infection. Once infection is confirmed, cultures should then be performed to identify the organism causing the infection to help select the appropriate treatment regimen.

Systemic antifungals are the most effective treatment for onychomycosis. Antifungals from the azole and allylamine classes are the most widely used oral medications for the treatment of onychomycosis. Terbinafine (Lamisil) is the most effective systemic agent available. Oral treatment of onychomycosis is the standard of care, however, drug interactions and risk of acute liver injury can limit their use. Difficulties in formulating topical treatment to penetrate the nail and reach the site of infection in the nail bed has hampered the development and the use of topical agents. Jublia is the first triazole antifungal for the treatment of onychomycosis. In 2 randomized trials, complete cure rate, defined as no evidence of fungal infection at week 52, was demonstrated in 15.2% to 17.8% of patients receiving efinaconazole (N=1236) compared with 3.3% to 5.5% receiving placebo (N=415) for the treatment of onychomycosis of the toenail. Jublia provided
an effective and well-tolerated treatment and may be the first topical treatment that can be considered a viable alternative to oral treatments.4

REFERENCES

CRITERIA FOR APPROVAL

1. Is the requested drug being prescribed for onychomycosis of the toenail(s) due to Trichophyton rubrum or Trichophyton mentagrophytes, which has been confirmed with a fungal diagnostic test (e.g., potassium hydroxide [KOH] preparation, fungal culture, or nail biopsy)?
   - Yes
   - No

2. Has the patient experienced an inadequate treatment response, intolerance, or contraindication to an oral antifungal therapy (e.g., terbinafine, itraconazole)?
   - Yes
   - No

Guidelines for Approval

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Mapping Instructions

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2. | Approve, 12 months | Deny | You do not meet the requirements of your plan. Your plan covers this drug when you have tried at least one oral medicine first and it did not work for you or you cannot use it. Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance, or contraindication to oral antifungals] |
SPECIALTY GUIDELINE MANAGEMENT

JUXTAPID (Lomitapide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Juxtapid is indicated as an adjunct to a low-fat diet and other lipid-lowering treatments, including LDL apheresis where available, to reduce low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), apolipoprotein B (apo B), and non-high-density lipoprotein cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH).

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of documentation supporting the diagnosis of homozygous familial hypercholesterolemia per Appendix A or B is necessary to initiate the prior authorization review.

III. CRITERIA FOR INITIAL APPROVAL

Homozygous familial hypercholesterolemia (HoFH)

Authorization for 6 months may be granted for members who meet all of the criteria listed below:

A. Member has a documented diagnosis of HoFH confirmed by genetic analysis or clinical criteria (See Appendices).

B. Prior to initiation of treatment with Juxtapid, patient is/was receiving a combination lipid-lowering regimen consisting of a high-intensity statin, ezetimibe, and evolocumab (Repatha), unless the member has known LDL-receptor negative mutations in both alleles.

C. Prior to initiation of treatment with Juxtapid, patient is/was experiencing an inadequate response to such a combination regimen, as demonstrated a treated LDL-C of greater than or equal to 100 mg/dL (or greater than or equal to 70 mg/dL with clinical atherosclerotic cardiovascular disease [ASCVD]), unless the member has known LDL-receptor negative mutations in both alleles.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members (including new members) who meet all initial authorization criteria and have achieved or maintained a LDL-C reduction greater than 20% from the levels immediately prior to initiation of treatment with Juxtapid.
V. APPENDICES

APPENDIX A. Diagnosis of Homozygous Familial Hypercholesterolemia

- Genetic confirmation
  - Mutations in both alleles at LDL receptor, ApoB, PCSK9 or LDL receptor adaptor protein gene locus
- Clinical diagnosis
  - Untreated LDL-C > 500 mg/dL OR unknown untreated LDL-C with treated LDL-C > 300 mg/dL **plus**
  - One of the following:
    - Tendon or cutaneous xanthomas at age 10 or younger
    - Diagnosis of familial hypercholesterolemia (FH) by Simon-Broome Diagnostic Criteria or Dutch Lipid Clinic Network Criteria (See Appendix B) in both parents
    - Evidence of FH in both parents with a history including any of the following:
      - Total cholesterol ≥ 310 mg/dL
      - Premature ASCVD (before 55 years in men and 60 years in women)
      - Tendon xanthoma
      - Sudden premature cardiac death

APPENDIX B: Diagnosis of familial hypercholesterolemia (FH)

A diagnosis of FH is made when one of the following diagnostic criteria is met:

- Genetic confirmation
  - An LDL-receptor mutation, familial defective apo B-100, or a PCSK9 gain-of-function mutation
- Simon-Broome Diagnostic Criteria for FH
  - Total cholesterol > 290 mg/dL or LDL-C > 190 mg/dL in patients over 16 years of age or total cholesterol > 260 mg/dl or LDL-C > 155 mg/dl in patients less than 16 years of age and one of the following
    - Tendon xanthomas in the patient, first (parent, sibling or child) or second degree relative (grandparent, uncle or aunt)
    - Family history of myocardial infarction in a first degree relative before the age of 60 or in a second degree relative before the age of 50
    - Total cholesterol greater than 290 mg/dl in an adult first or second degree relative
    - Total cholesterol greater than 260 mg/dl in a child, brother, or sister aged younger than 16 years
- Dutch Lipid Clinic Network Criteria for FH
  - Total score > 5 points

VI. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

JYNARQUE (tolvaptan)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Jynarque is indicated to slow kidney function decline in adults at risk of rapidly progressing autosomal dominant polycystic kidney disease (ADPKD).

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of autosomal dominant polycystic kidney disease (ADPKD) when all of the following criteria are met:

A. Diagnosis of autosomal dominant polycystic kidney disease has been confirmed by ultrasonography, computed tomography (CT), magnetic resonance imaging (MRI) or genetic testing.

B. The member has or is at risk for rapidly progressing disease as confirmed by any of the following:
   1. An annual estimated glomerular filtration rate (eGFR) decline of at least 5 mL/min/1.73 m² in 1 year and/or eGFR decline of at least 2.5 mL/min/1.73 m² per year over a period of 5 years
   2. A total kidney volume (TKV) increase of greater than 5% per year confirmed by at least 3 repeated ultrasound or MRI measurements taken at least 6 months apart
   3. Presence of truncating PKD1 mutation accompanied by early onset of clinical symptoms (e.g., hypertension before 35 years of age, first urological event [macroscopic hematuria, flank pain or cyst infection] before 35 years of age)
   4. Height-adjusted total kidney volume compatible with Mayo class 1C, 1D, or 1E disease
   5. Patient is less than 45 years of age with a kidney length of greater than 16.5 cm as assessed by ultrasound

C. The member's estimated glomerular filtration rate (eGFR) is greater than or equal to 25 mL/min/1.73m².

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when the member has demonstrated a beneficial response to Jynarque therapy (e.g., slowed kidney function decline, decreased kidney pain) and the member's estimated glomerular filtration rate (eGFR) is greater than or equal to 25 mL/min/1.73m².

IV. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

KADCYLA (ado-trastuzumab emtansine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Metastatic Breast Cancer (MBC)
   Kadcyla, as a single agent, is indicated for the treatment of patients with human epidermal growth factor receptor 2 (HER2)-positive, metastatic breast cancer who previously received trastuzumab and a taxane, separately or in combination. Patients should have either received prior therapy for metastatic disease, or developed disease recurrence during or within six months of completing adjuvant therapy.

2. Early Breast Cancer (EBC)
   Kadcyla, as a single agent, is indicated for the adjuvant treatment of patients with HER2-positive early breast cancer who have residual invasive disease after neoadjuvant taxane and trastuzumab-based treatment.

B. Compendial Uses

1. Single-agent therapy for recurrent or stage IV (M1) HER2-positive breast cancer
2. Non-small cell lung cancer with HER2 mutations

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Breast cancer

1. Authorization of 12 months may be granted for treatment of HER2-positive metastatic or recurrent breast cancer.
2. Authorization of 12 months may be granted for adjuvant treatment of HER2-positive early breast cancer who have residual invasive disease after neoadjuvant taxane and trastuzumab-based treatment.

B. Non-small cell lung cancer
   Authorization of 12 months may be granted for treatment of lung cancer with HER2 mutations.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.
IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

KALBITOR (ecallantide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Treatment of acute attacks of hereditary angioedema (HAE) in patients 12 years of age and older

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. C4 levels and C1 inhibitor functional and antigenic protein levels
B. F12, angiopoietin-1 or plasminogen gene mutation testing, if applicable
C. Chart notes confirming family history of angioedema, if applicable

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of acute hereditary angioedema attacks when the requested medication will not be used in combination with Berinert, Firazyr, or Ruconest and either of the following criteria is met:
A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing:
   1. C1 inhibitor (C1-INH) antigenic level is below the lower limit of normal as defined by the laboratory performing the test, or
   2. Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test)
B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
   1. Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing, or
   2. Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy when all of the following criteria are met:
A. Member meets the criteria for initial approval.
B. Member has experienced reduction in severity and/or duration of attacks when they use the requested medication to treat an acute attack.
V. REFERENCES

ENHANCED SPECIALTY GUIDELINE MANAGEMENT

KALBITOR (ecallantide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Treatment of acute attacks of hereditary angioedema (HAE) in patients 12 years of age and older

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. C4 levels and C1 inhibitor functional and antigenic protein levels
B. F12, angiopoietin-1 or plasminogen gene mutation testing, if applicable
C. Chart notes confirming family history of angioedema, if applicable

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of acute hereditary angioedema attacks when the requested medication will not be used in combination with Berinert, Firazyr, or Ruconest and either of the following criteria is met:

A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing:
   1. C1 inhibitor (C1-INH) antigenic level is below the lower limit of normal as defined by the laboratory performing the test, or
   2. Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test).
B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
   1. Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing, or
   2. Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy when all of the following criteria are met:

A. Member meets the criteria for initial approval.
B. Member has experienced reduction in severity and/or duration of attacks when they use the requested medication to treat an acute attack.
V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

KALYDECO (ivacaftor)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Kalydeco is a cystic fibrosis transmembrane conductance regulator (CFTR) potentiator indicated for the treatment of cystic fibrosis (CF) in patients age 6 months and older who have one mutation in the CFTR gene that is responsive to ivacaftor potentiation based on clinical and/or in vitro assay data.

If the patient’s genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of CFTR mutation followed by verification with bi-directional sequencing when recommended by the mutation test instructions for use.

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review: genetic testing report confirming the presence of the appropriate CFTR gene mutation.

III. CRITERIA FOR INITIAL APPROVAL

Cystic Fibrosis
Indefinite authorization may be granted for treatment of cystic fibrosis when all of the following criteria are met:
A. Genetic testing was conducted to detect a mutation in the CFTR gene.
C. The member is at least 6 months of age.
D. Kalydeco will not be used in combination with Orkambi or Symdeko.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

KANUMA (sebelipase alfa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Kanuma is indicated for the treatment of patients with a diagnosis of Lysosomal Acid Lipase (LAL) deficiency.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Lysosomal acid lipase (LAL) deficiency
Indefinite authorization may be granted for treatment of LAL deficiency when the diagnosis of LAL deficiency was confirmed by enzyme assay demonstrating a deficiency of lysosomal acid lipase enzyme activity or by genetic testing.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

**PRIOR AUTHORIZATION CRITERIA**

<table>
<thead>
<tr>
<th>BRAND NAME*</th>
<th>KERYDIN (tavaborole topical solution)</th>
</tr>
</thead>
</table>

**Status:** CVS Caremark Criteria  
**Type:** Initial Prior Authorization  
**Ref #:** 1169-A  

*Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

**FDA-APPROVED INDICATIONS**

Kerydin (tavaborole) topical solution, 5% is an oxaborole antifungal indicated for the treatment of onychomycosis of the toenails due to Trichophyton rubrum or Trichophyton mentagrophytes.

**COVERAGE CRITERIA**

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for onychomycosis of the toenail(s) due to Trichophyton rubrum or Trichophyton mentagrophytes, which has been confirmed with a fungal diagnostic test (e.g., potassium hydroxide [KOH] preparation, fungal culture, or nail biopsy)

  **AND**

- The patient has experienced an inadequate treatment response, intolerance, or contraindication to an oral antifungal therapy (e.g., terbinafine, itraconazole)

**RATIONALE**

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Kerydin (tavaborole) topical solution, 5% is an oxaborole antifungal indicated for the treatment of onychomycosis of the toenails due to Trichophyton rubrum or Trichophyton mentagrophytes. Kerydin is to be applied to affected toenails once daily for 48 weeks. Kerydin should be applied to the entire toenail surface and under the tip of each toenail being treated. Kerydin is for topical use only and not for oral, ophthalmic, or intravaginal use.

Accurate diagnosis of onychomycosis involves physical and microscopic examination and culture. Only 50% of nail problems are caused by onychomycosis, and clinical diagnosis by physical examination alone can be inaccurate. When onychomycosis is suspected, samples should be taken to conduct diagnostic tests. Samples are then prepared with potassium hydroxide (KOH) solution to be viewed under a microscope to look for the presence of a fungal infection. Once infection is confirmed, cultures should then be performed to identify the organism causing the infection to help select the appropriate treatment regimen.

Systemic antifungals are the most effective treatment for onychomycosis. Antifungals from the azole and allylamine classes are the most widely used oral medications for the treatment of onychomycosis. Terbinafine (Lamisil) is the most effective systemic agent available. Oral treatment of onychomycosis is the standard of care, however, drug interactions and risk of acute liver injury can limit their use. Difficulties in formulating topical treatment to penetrate the nail and reach the site of infection in the nail bed has hampered the development and the use of topical agents. In 2 randomized trials, complete cure rate, defined as no evidence of fungal infection at week 52, was demonstrated in 6.5% and 9.1% of patients receiving tavaborole compared with 0.5% and 1.5% receiving placebo for the treatment of onychomycosis of the toenail.
**REFERENCES**


Written by: UM Development (PL/WW)
Date Written: 07/2014
Revised: (MS) 05/2015; (KM) 05/2016; (JH) 04/2017 (no clinical changes); (KC) 04/2018), (ME) 02/2019 (no clinical changes)
Reviewed: Medical Affairs (LMS) 07/2014; (KU) 05/2015; (ME) 05/2016

### CRITERIA FOR APPROVAL

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</thead>
<tbody>
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<td>1</td>
<td>Is the requested drug being prescribed for onychomycosis of the toenail(s) due to Trichophyton rubrum or Trichophyton mentagrophytes, which has been confirmed with a fungal diagnostic test (e.g., potassium hydroxide [KOH] preparation, fungal culture, or nail biopsy)?</td>
<td>Yes</td>
<td>No</td>
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<td>2</td>
<td>Has the patient experienced an inadequate treatment response, intolerance, or contraindication to an oral antifungal therapy (e.g., terbinafine, itraconazole)?</td>
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### Guidelines for Approval

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<thead>
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<th>Duration of Approval</th>
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</tr>
<tr>
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</tr>
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</tr>
<tr>
<td>2</td>
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</table>

### Mapping Instructions

<table>
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<tr>
<th>Yes</th>
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<th>DENIAL REASONS – DO NOT USE FOR MEDICARE PART D</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Go to 2</td>
<td>Deny You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: - You have a specific fungal infection of the toenail(s) - You had a test to confirm your toenail fungus Your request has been denied based on the information we have. [Short Description: No approvable diagnosis, no confirmation of diagnosis]</td>
</tr>
<tr>
<td>2.</td>
<td>Approve, 12 months</td>
<td>Deny You do not meet the requirements of your plan. Your plan covers this drug when you have tried at least one oral medicine first and it did not work for you or you cannot use it. Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance, or contraindication to an oral antifungal]</td>
</tr>
</tbody>
</table>
POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Treatment of primary hyperkalemic periodic paralysis, primary hypokalemic periodic paralysis, and related variants.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Primary Hypokalemic Periodic Paralysis
Authorization of 60 days may be granted to members who are initiating Keveyis therapy when the following criteria is met:
1. The diagnosis was supported by at least one of the following:
   a. Genetic test results or
   b. Patient has a family history of primary hypokalemic periodic paralysis, or
   c. Patient’s attacks are associated with hypokalemia AND both Andersen-Tawil syndrome and thyrotoxic periodic paralysis have been ruled out.
2. Trial with suboptimal response to treatment with acetazolamide

B. Primary Hyperkalemic Periodic Paralysis
Authorization of 60 days may be granted to members who are initiating Keveyis therapy when the following criteria is met:
1. The diagnosis was supported by at least one of the following:
   a. Genetic test results, or
   b. Patient has a family history of primary hyperkalemic periodic paralysis, or
   c. Patient’s attacks are associated with hyperkalemia AND Andersen-Tawil syndrome has been ruled out.
2. Trial with suboptimal response to treatment with acetazolamide

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted to members who have demonstrated a response to Keveyis therapy as demonstrated by an improvement in their condition (e.g. decrease in the number or severity of attacks).
IV. REFERENCE

SPECIALTY GUIDELINE MANAGEMENT

KEVZARA (sarilumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Kevzara is indicated for treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to one or more disease-modifying antirheumatic drugs (DMARDs)

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Moderately to severely active rheumatoid arthritis (RA)

A. Authorization of 24 months may be granted for members who have previously received Kevzara or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) indicated for moderately to severely active rheumatoid arthritis.

B. Authorization of 24 months may be granted for treatment of moderately to severely active RA when any of the following criteria is met:
   1. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
   2. Member has an intolerance or contraindication to methotrexate (see Appendix).

III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Kevzara as evidenced by low disease activity or improvement in signs and symptoms of RA.

IV. OTHER

Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB).

Note: Members who have received Kevzara or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) are exempt from requirements related to TB screening in this Policy.
V. APPENDIX: Examples of Contraindications to Methotrexate
1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy (male or female)
10. Renal impairment
11. Significant drug interaction

VI. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

KEYTRUDA (pembrolizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Melanoma
   i. Keytruda is indicated for the treatment of patients with unresectable or metastatic melanoma.
   ii. Keytruda is indicated for the adjuvant treatment of patients with melanoma with involvement of lymph node(s) following complete resection.

2. Non-Small Cell Lung Cancer
   i. Keytruda, as a single agent, is indicated for the first-line treatment of patients with stage III non-small cell lung cancer (NSCLC), who are not candidates for surgical resection or definitive chemoradiation, or metastatic NSCLC, and whose tumors express PD-L1 [Tumor Proportion Score (TPS) ≥1%] as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations.
   ii. Keytruda, as a single agent, is indicated for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥1%) as determined by an FDA approved test, with disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Keytruda.
   iii. Keytruda, in combination with pemetrexed and platinum chemotherapy, is indicated for the first-line treatment of patients with metastatic nonsquamous NSCLC, with no EGFR or ALK genomic tumor aberrations.
   iv. Keytruda, in combination with carboplatin and either paclitaxel or paclitaxel protein-bound, as first-line treatment of patients with metastatic squamous NSCLC.

3. Head and Neck Squamous Cell Cancer
   Keytruda is indicated for the treatment of patients with recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) with disease progression on or after platinum-containing chemotherapy.

4. Classical Hodgkin Lymphoma
   Keytruda is indicated for the treatment of adult and pediatric patients with refractory classical Hodgkin lymphoma (cHL), or who have relapsed after three or more prior lines of therapy.

5. Urothelial Carcinoma (Bladder cancer, Upper Genitourinary tract tumors, Urothelial carcinoma of the prostate, Primary carcinoma of the urethra)
   Keytruda is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who:
   i. Are not eligible for cisplatin-containing chemotherapy and whose tumors express PD-L1 [Combined Positive Score (CPS) ≥ 10] as determined by an FDA-approved test, or
ii. Are not eligible for any platinum-containing chemotherapy regardless of PD-L1 status, or
iii. Have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

6. Microsatellite Instability-High Cancer
Keytruda is indicated for the treatment of adult and pediatric patients with unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient
i. Solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options, or
ii. Colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.

Limitation of Use: The safety and effectiveness of Keytruda in pediatric patients with MSI-H central nervous system cancers have not been established.

7. Gastric Carcinoma
Keytruda is indicated for the treatment of patients with recurrent, locally advanced, metastatic gastric or gastroesophageal junction adenocarcinoma whose tumors express PD-L1 [Combined Positive Score (CPS) ≥ 1] as determined by an FDA approved test, with disease progression on or after two or more prior lines of therapy including fluoropyrimidine and platinum containing chemotherapy and if appropriate, HER2/neu targeted therapy.

8. Cervical Cancer
Keytruda is indicated for the treatment of patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy whose tumor express PD-L1 [Combined Positive Score (CPS) ≥ 1] as determined by an FDA approved test

9. Primary Mediastinal large B-cell Lymphoma (PMBCL)
Keytruda is indicated for the treatment of adult and pediatric patients with refractory PMBCL, or who have relapsed after 2 or more prior lines of therapy.

Limitation of Use: Keytruda is not recommended for treatment of patients with PMBCL who require urgent cytoreductive therapy.

10. Hepatocellular Carcinoma (HCC)
Keytruda is indicated for the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

11. Merkel Cell Carcinoma (MCC)
Keytruda is indicated for the treatment of adult and pediatric patients with recurrent locally advanced or metastatic Merkel cell carcinoma.

12. Renal Cell Carcinoma (RCC)
Keytruda is indicated in combination with axitinib, for the first-line treatment of patients with advanced renal cell carcinoma.

B. Compendial Uses
1. Non-small cell lung cancer
2. Unresectable advanced or metastatic microsatellite instability-high colorectal cancer
3. Malignant pleural mesothelioma
4. Gastric carcinoma
5. Colorectal cancer
6. Epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer
7. Uveal melanoma
8. Esophageal and Esophagogastric Junction cancers
9. Bone cancer
   i. Ewing’s sarcoma
   ii. Osteosarcoma
10. Testicular cancer
11. Endometrial carcinoma
12. Anal carcinoma
13. Adrenal gland tumors
14. Penile cancer
15. Central Nervous System (CNS) brain metastases in patients with melanoma or NSCLC
17. Pancreatic adenocarcinoma
18. Hepatobiliary cancers
   i. Extrahepatic cholangiocarcinoma
   ii. Intrahepatic cholangiocarcinoma
   iii. Gallbladder cancer
19. Squamous cell vulvar cancer

All other indications are considered experimental/investigational and are not a covered benefit.

II. EXCLUSIONS

Coverage will not be provided for pediatric members with microsatellite instability-high (MSI-H) central nervous system cancers.

III. CRITERIA FOR INITIAL APPROVAL

A. Melanoma

Authorization of 12 months may be granted for treatment of melanoma in either of the following settings:
1. Treatment of unresectable or metastatic melanoma.
2. Adjuvant treatment of members with melanoma with involvement of lymph node(s) following complete resection.

B. Non-small Cell Lung Cancer (NSCLC)

1. Authorization of 12 months may be granted for treatment of metastatic NSCLC in any of the following settings:
   i. First-line treatment of nonsquamous NSCLC:
      a. The member’s EGFR, ALK and ROS1 genomic tumor markers are negative or unknown, AND
      b. Keytruda will be used as a single agent or in combination with both of the following:
         1. Pemetrexed
         2. Carboplatin or cisplatin
   ii. First-line treatment of squamous NSCLC:
      a. Keytruda will be used in combination with carboplatin and paclitaxel or albumin-bound paclitaxel, OR
      b. Member meets both of the following:
         1. The member’s EGFR, ALK and ROS1 genomic tumor markers are negative or unknown
         2. Keytruda will be used as a single agent or in combination with both of the following:
            a. Carboplatin or cisplatin
b. Paclitaxel or albumin-bound paclitaxel

iii. Maintenance therapy: Keytruda was used as part of first-line chemotherapy.

iv. Subsequent therapy
   1. Following targeted therapy if any of the following genomic tumor markers are positive: EGFR, ALK, or ROS1, OR
   2. Following cytotoxic chemotherapy.

2. Authorization of 12 months may be granted for the first-line treatment of stage III NSCLC which is not appropriate for surgical resection or definitive chemoradiation when Keytruda will be used as a single agent and the member’s EGFR, ALK and ROS1 genomic tumor markers are negative or unknown.

C. Head and Neck Cancer
   Authorization of 12 months may be granted for the treatment of members with recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) with disease progression on or after platinum-containing chemotherapy.

D. Classical Hodgkin Lymphoma
   Authorization of 12 months may be granted for treatment of refractory or relapsed classical Hodgkin lymphoma.

E. Urothelial Carcinoma (Bladder cancer, upper genitourinary tract tumors, urothelial carcinoma of the prostate, primary carcinoma of the urethra)
   Authorization of 12 months may be granted for treatment of locally advanced or metastatic urothelial carcinoma when any of the following criteria is met:
   1. Member is not eligible for cisplatin-containing chemotherapy and whose tumors express PD-L1 [Combined Positive Score (CPS) ≥ 10].
   2. Member is not eligible for platinum-containing chemotherapy.
   3. Member experienced disease progression during or following platinum-containing chemotherapy.
   4. Member experienced disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

F. Microsatellite Instability-High Cancer
   Authorization of 12 months may be granted for treatment of unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient solid tumors when either of the following criteria are met:
   1. The member has colorectal cancer
   2. For other solid tumors: Member experienced disease progression following prior treatment and has no satisfactory alternative treatment options.

G. Malignant Pleural Mesothelioma
   Authorization 12 months may be granted for treatment of malignant pleural mesothelioma.

H. Merkel Cell Carcinoma
   Authorization of 12 months may be granted for treatment of Merkel cell carcinoma.

I. Gastric Carcinoma
   Authorization of 12 months may be granted for treatment of recurrent locally advanced, metastatic gastric or gastroesophageal junction adenocarcinoma when either of the following criteria are met:
   1. Keytruda is being used as second-line or subsequent therapy for a tumor with microsatellite instability-high (MSI-H) or deficient mismatch repair (dMMR), OR
   2. Keytruda is being used as third-line or subsequent therapy for a PD-L1 positive tumor [Combined Positive Score (CPS) ≥ 1].
J. Cervical Cancer
Authorization of 12 months may be granted for the treatment of recurrent or metastatic cervical cancer when all of the following criteria are met:
1. Tumor expresses PD-L1 [Combined Positive Score (CPS) greater than or equal to 1].
2. Member has experienced disease progression on or after chemotherapy.

K. Epithelial Ovarian Cancer, Fallopian Tube Cancer, Primary Peritoneal Cancer
Authorization of 12 months may be granted for the treatment of epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer.

L. Uveal Melanoma
Authorization of 12 months may be granted for treatment of uveal melanoma.

M. Esophageal and Esophagogastric Junction Cancers
Authorization of 12 months may be granted for treatment of esophageal and esophagogastric junction cancer.

N. Bone Cancer
Authorization of 12 months may be granted for the treatment of Ewing’s sarcoma and osteosarcoma.

O. Testicular Cancer
Authorization of 12 months may be granted for the treatment of testicular cancer.

P. Endometrial Carcinoma
Authorization of 12 months may be granted for the treatment of endometrial carcinoma.

Q. Anal Carcinoma
Authorization of 12 months may be granted for the treatment of anal cancer.

R. Adrenal Gland Tumors
Authorization of 12 months may be granted for the treatment of adrenal gland tumors.

S. Penile Cancer
Authorization of 12 months may be granted for the treatment of penile cancer.

T. CNS Brain Metastases
Authorization of 12 months may be granted for the treatment of CNS brain metastases in members with melanoma or non-small cell lung cancer (NSCLC).

U. Non-Hodgkin’s Lymphoma (including Primary Mediastinal Large B-Cell Lymphoma)
Authorization of 12 months may be granted for the treatment of non-Hodgkin’s lymphoma.

V. Pancreatic Adenocarcinoma
Authorization of 12 months may be granted for the treatment of pancreatic adenocarcinoma.

W. Hepatobiliary Cancers
Authorization of 12 months may be granted for the treatment of intrahepatic and extrahepatic cholangiocarcinoma and gallbladder cancer.

X. Hepatocellular Carcinoma (HCC)
Authorization of 12 months may be granted for the treatment of members with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

Y. Squamous Cell Vulvar Cancer
Authorization of 12 months may be granted for the treatment of members with squamous cell vulvar cancer.

Z. Renal Cell Carcinoma
Authorization of 12 months may be granted for the treatment of members with renal cell carcinoma when Keytruda will be used in combination with axitinib.

IV. CONTINUATION OF THERAPY

A. Adjuvant treatment of melanoma
Authorization of up to 12 months total may be granted for all members (including new members) who meet all initial authorization criteria.

B. All other indications
Authorization of 12 months may be granted for all members (including new members) who meet all initial authorization criteria.

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

KINERET (anakinra)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Moderately to severely active rheumatoid arthritis (RA)
   2. Cryopyrin-Associated Periodic Syndromes (CAPS)
      a. Neonatal-Onset Multisystem Inflammatory Disease (NOMID)

B. Compendial Uses
   1. Systemic juvenile idiopathic arthritis (sJIA)
   2. Adult-onset Still’s disease
   3. B-cell lymphomas – multicentric Castleman’s disease
   4. Recurrent pericarditis
   5. Hyperimmunoglobulin D syndrome [Mevalonate Kinase Deficiency (MKD)]
   6. Schnitzler syndrome

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderately to Severely Active Rheumatoid Arthritis (RA)
   Authorization of 24 months may be granted for members who meet ANY of the following criteria:
   1. Member has experienced an inadequate response to at least a 3-month trial of a biologic DMARD or a targeted synthetic DMARD (e.g., Xeljanz)
   2. Member has experienced intolerance to a biologic or targeted synthetic DMARD

B. Adult Onset Still’s Disease
   Authorization of 24 months may be granted for members with Adult Onset Still’s disease.

C. Active Systemic Juvenile Idiopathic Arthritis (sJIA)
   1. Authorization of 24 months may be granted for the treatment of sJIA for members who have received Actemra or Ilaris in a paid claim through a pharmacy or medical benefit within the previous 120 days.
   2. Authorization of 24 months may be granted for the treatment of active sJIA for members who have had an inadequate response to a trial of nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, methotrexate, or leflunomide.
   3. Authorization of 24 months may be granted for the treatment of sJIA for members who have a physician global assessment score greater than or equal to 5.

D. Neonatal-Onset Multisystem Inflammatory Disease (NOMID)
Authorization of 24 months may be granted for the treatment of cryopyrin-associated periodic syndromes (CAPS), including NOMID (also known as chronic infantile neurologic cutaneous and articular syndrome [CINCA]).

E. Recurrent Pericarditis
Authorization of 12 months may be granted for the treatment of recurrent pericarditis for members who have failed a first-line therapy agent (i.e., colchicine).

F. B-cell Lymphomas – Multicentric Castleman’s Disease
Authorization of 12 months may be granted for the treatment of multicentric Castleman’s disease.

G. Hyperimmunoglobulin D Syndrome [Mevalonate Kinase Deficiency (MKD)]
Authorization of 24 months may be granted for the treatment of hyperimmunoglobulin D syndrome.

H. Schnitzler syndrome
Authorization of 12 months may be granted for the treatment of Schnitzler syndrome.

III. CONTINUATION OF THERAPY

A. Adult Onset Still’s Disease, Rheumatoid Arthritis and Juvenile Idiopathic Arthritis
Authorization of 24 months may be granted for all members (including new members) who have achieved or maintained a positive clinical response after at least 3 months of therapy with Kineret as evidenced by low disease activity or improvement in signs and symptoms of the condition.

B. Neonatal-Onset Multisystem Inflammatory Disease (NOMID), Castleman’s disease, Recurrent Pericarditis, Hyperimmunoglobulin D Syndrome, and Schnitzler syndrome
All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria.

IV. APPENDIX: Examples of Contraindications to Methotrexate
1. History of intolerance or adverse event
2. Alcoholic liver disease or other chronic liver disease
3. Elevated liver transaminases
4. Interstitial pneumonitis or clinically significant pulmonary fibrosis
5. Renal impairment
6. Current pregnancy or planning pregnancy
7. Breastfeeding
8. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
9. Myelodysplasia
10. Hypersensitivity
11. Significant drug interaction

V. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

KISQALI (ribociclib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

1. Kisqali is indicated in combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of pre/perimenopausal or postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer.

2. Kisqali is indicated in combination with fulvestrant for the treatment of postmenopausal women with (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer, as initial endocrine based therapy or following disease progression on endocrine therapy.

B. Compendial Uses

Kisqali is indicated in combination with tamoxifen for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Breast cancer

Authorization of 12 months may be granted to members for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer when Kisqali is used in combination with an aromatase inhibitor, fulvestrant or tamoxifen.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

KISQALI FEMARA CO-PACK (ribociclib tablets; letrozole tablets)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

The Kisqali Femara Co-Pack is indicated as initial endocrine-based therapy for the treatment of pre/perimenopausal or postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Breast cancer

Authorization of 12 months may be granted to members for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

KORLYM (mifepristone)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Korlym is a cortisol receptor blocker indicated to control hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing’s syndrome who have type 2 diabetes mellitus or glucose intolerance and have failed surgery or are not candidates for surgery.

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. For initial requests: pretreatment hemoglobin A1C level
B. For continuation of therapy: current hemoglobin A1C level

III. CRITERIA FOR INITIAL APPROVAL

Cushing’s syndrome/disease
Authorization of 6 months may be granted for treatment of Cushing’s syndrome/disease when all of the following criteria are met:
A. Member has type 2 diabetes mellitus or glucose intolerance
B. Korlym is being prescribed to control hyperglycemia secondary to hypercortisolism
C. Member has failed to achieve adequate glycemic control despite individualized diabetic management
D. Member has had surgery that was not curative OR member is not a candidate for surgery
E. If the member is able to become pregnant, a negative pregnancy test is required before initiating therapy

IV. CONTINUATION OF THERAPY

Cushing’s syndrome/disease
Authorization of 12 months for continuation of therapy may be granted if the member has experienced improved glycemic control as evidenced by decreased hemoglobin A1C levels.

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

Policy

KRYSTEXXA (pegloticase)

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Krystexxa is indicated for the treatment of chronic gout in adult patients refractory to conventional therapy.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Chronic gout

Authorization of 12 months may be granted for members with a diagnosis of chronic gout when ALL of the following criteria are met:

A. Krystexxa will NOT be used concomitantly with oral urate-lowering therapies
B. Member has had an inadequate response to or a clinical reason for not completing at least a three-month trial (see Appendix) with the following medications at the medically appropriate maximum doses:
   1. Allopurinol or febuxostat
   2. Probenecid (alone or in combination with allopurinol or febuxostat)

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) with a diagnosis of chronic gout that meet ALL initial authorization criteria and have NOT had two consecutive uric acid levels above 6 mg/dL since starting treatment with Krystexxa.

IV. APPENDIX: Clinical reasons for not completing a three-month trial with allopurinol, febuxostat, and probenecid (examples):

A. Member experienced a severe allergic reaction to the medication
B. Member experienced toxicity with the medication
C. Member could not tolerate the medication
D. Member’s current medication regimen has a significant drug interaction
E. Member has severe renal dysfunction (allopurinol)
F. Member has known blood dyscrasias or uric acid kidney stones (probenecid)
G. Member has renal insufficiency (i.e., glomerular filtration rate 30 mL/minute or less) (probenecid)
H. Member has end stage renal impairment (febuxostat)
V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

KUVAN (sapropterin dihydrochloride)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Kuvan is indicated to reduce blood phenylalanine (Phe) levels in patients with hyperphenylalaninemia (HPA) due to tetrahydrobiopterin- (BH4-) responsive phenylketonuria (PKU). Kuvan is to be used in conjunction with a Phe-restricted diet.

B. Compendial Uses

1. Autosomal dominant guanine triphosphate cyclohydrolase deficiency (Segawa disease)
2. Autosomal recessive guanine (GTP) cyclohydrolase deficiency
3. 6-pyruvoyl-tetrahydropterin synthase (6-PTS) deficiency
4. Sepiapterin reductase deficiency
5. Dihydropteridine reductase (DHPR) deficiency
6. Pterin-4a-carbinolamine dehydratase deficiency (also called primapterinuria)

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Phenylketonuria (PKU)

1. Authorization of 2 months may be granted for members requesting a therapeutic trial with Kuvan when the pretreatment, including before dietary management, phenylalanine level was greater than 6 mg/dL (360 micromol/L).

2. Authorization of indefinite approval may be granted following a therapeutic trial with Kuvan when the member’s therapeutic trial meets either of the following:
   a. Member experienced a reduction in blood phenylalanine level of at greater than or equal to 30% from baseline during the therapeutic trial with Kuvan.
   b. Member has demonstrated an improvement in neuropsychiatric symptoms during the therapeutic trial with Kuvan.

B. Biopterin Metabolic Defects

Authorizations of indefinite approval may be granted for members who have any of the following biopterin metabolic defects:

1. Autosomal dominant guanine triphosphate cyclohydrolase deficiency (Segawa disease)
2. Autosomal recessive guanine (GTP) cyclohydrolase deficiency
3. 6-pyruvoyl-tetrahydropterin synthase (6-PTS) deficiency
4. Sepiapterin reductase deficiency
5. Dihydropteridine reductase (DHPR) deficiency
6. Pterin-4a-carbinolamine dehydralase deficiency (also called primapterinuria)

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

KYMRIAH (tisagenlecleucel)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Pediatric and Young Adult Relapsed or Refractory (r/r) B-cell Acute Lymphoblastic Leukemia (ALL) Patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse.

2. Adult Relapsed or Refractory (r/r) Diffuse Large B-cell Lymphoma

   Adult patients with relapsed or refractory (r/r) large B-cell lymphoma after two or more lines of systemic therapy including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (NOS), high grade B-cell lymphoma and DLBCL arising from follicular lymphoma.

   Limitation of Use: Kymriah is not indicated for treatment of patients with primary central nervous system lymphoma.

B. Compendial Uses

1. Acquired immunodeficiency syndrome (AIDS)-related diffuse large B-cell lymphoma
2. Diffuse large B-cell lymphoma
3. Human herpesvirus 8 (HHV8)-positive diffuse large B-cell lymphoma, NOS
4. Monomorphic post-transplant lymphoproliferative disorder (B-cell type)
5. Primary mediastinal large B-cell lymphoma

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Testing or analysis confirming CD19 protein on the surface of the B-cell

III. CRITERIA FOR INITIAL APPROVAL

A. Pediatric and Young Adult Relapsed or Refractory (r/r) B-cell Acute Lymphoblastic Leukemia (ALL)

   Authorization of 3 months may be granted for treatment of B-cell precursor acute lymphoblastic leukemia (ALL) in patients less than or equal to 25 years of age when all of the following criteria are met:

   1. The disease is refractory to treatment or in second or later relapse.
   2. The member has not received a previous treatment course of Kymriah or another CD19-directed chimeric antigen receptor (CAR) T-cell therapy.
   3. The B-cells must be CD19-positive as confirmed by testing or analysis
4. Member meets one of the following:
   a. Member has Philadelphia chromosome-positive disease and failed at least two tyrosine kinase inhibitors (TKI) (e.g., imatinib, dasatinib, nilotinib, bosutinib, ponatinib).
   b. Member has Philadelphia chromosome-negative disease.

B. Adult B-cell Lymphomas

Authorization of 3 months may be granted for treatment of B-cell lymphomas in members 18 years of age or older when all of the following criteria are met:

1. Member has any of the following B-cell lymphoma subtypes:
   a. Diffuse large B-cell lymphoma (DLBCL) arising from follicular lymphoma (also known as follicular lymphoma with histologic transformation to DLBCL)
   b. Diffuse large B-cell lymphoma
   c. Primary mediastinal large B-cell lymphoma
   d. High-grade B-cell lymphoma (high-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 [double/triple hit lymphoma], high-grade B-cell lymphoma, NOS)
   e. Acquired immunodeficiency syndrome (AIDS)-related diffuse large B-cell lymphoma
   f. Human herpesvirus 8 (HHV8)-positive diffuse large B-cell lymphoma, NOS
   g. Monomorphic post-transplant lymphoproliferative disorder (B-cell type)

2. The member does not have primary central nervous system lymphoma.

3. The member has not received a previous treatment course of Kymriah or another CD19-directed chimeric antigen receptor (CAR) T-cell therapy.

4. The B-cells must be CD19-positive as confirmed by testing or analysis

5. For diffuse large B-cell lymphoma arising from follicular lymphoma: member received prior treatment with two or more chemoimmunotherapy regimens which included at least one anthracycline or anthracenedione-based regimen, unless contraindicated.

6. For all other B-cell lymphoma subtypes: member has partial response following second-line therapy OR the disease is in second relapse or greater.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

KYNAMRO (mipomersen)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Kynamro is indicated as an adjunct to lipid-lowering medications and diet to reduce low density lipoprotein-cholesterol (LDL-C), apolipoprotein B (apo B), total cholesterol, and non-high density lipoprotein-cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH).

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of documentation supporting the diagnosis of homozygous familial hypercholesterolemia per Appendix A or B is necessary to initiate the prior authorization review.

III. CRITERIA FOR INITIAL APPROVAL

Homozygous familial hypercholesterolemia (HoFH)
Authorization for 6 months may be granted for members who meet all of the criteria listed below:
A. Member has a documented diagnosis of HoFH confirmed by genetic analysis or clinical criteria (See Appendices).
B. Prior to initiation of treatment with Kynamro, patient is/was receiving a combination lipid-lowering regimen consisting of a high-intensity statin, ezetimibe, and evolocumab (Repatha), unless the member has known LDL-receptor negative mutations in both alleles.
C. Prior to initiation of treatment with Kynamro, patient is/was experiencing an inadequate response to such a combination regimen, as demonstrated a treated LDL-C of greater than or equal to 100 mg/dL (or greater than or equal to 70 mg/dL with clinical atherosclerotic cardiovascular disease [ASCVD]), unless the member has known LDL-receptor negative mutations in both alleles.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members (including new members) who meet all initial authorization criteria and have achieved or maintained a LDL-C reduction greater than 20% from the levels immediately prior to initiation of treatment with Kynamro.

V. APPENDICES

APPENDIX A. Diagnosis of Homozygous Familial Hypercholesterolemia
• Genetic confirmation
  o Mutations in both alleles at LDL receptor, ApoB, PCSK9 or LDL receptor adaptor protein gene locus

• Clinical diagnosis
  o Untreated LDL-C > 500 mg/dL OR unknown untreated LDL-C with treated LDL-C > 300 mg/dL plus
    o One of the following:
      ▪ Tendon or cutaneous xanthomas at age 10 or younger
      ▪ Diagnosis of familial hypercholesterolemia (FH) by Simon-Broome Diagnostic Criteria or Dutch Lipid Clinic Network Criteria (See Appendix B) in both parents
      ▪ Evidence of FH in both parents with a history including any of the following:
        • Total cholesterol ≥ 310 mg/dL
        • Premature ASCVD (before 55 years in men and 60 years in women)
        • Tendon xanthoma
        • Sudden premature cardiac death

APPENDIX B: Diagnosis of familial hypercholesterolemia (FH)
A diagnosis of FH is made when one of the following diagnostic criteria is met:
• Genetic confirmation
  o An LDL-receptor mutation, familial defective apo B-100, or a PCSK9 gain-of-function mutation

• Simon-Broome Diagnostic Criteria for FH
  o Total cholesterol > 290 mg/dL or LDL-C > 190 mg/dL in patients over 16 years of age or total cholesterol > 260 mg/dL or LDL-C > 155 mg/dL in patients less than 16 years of age and one of the following
    ▪ Tendon xanthomas in the patient, first (parent, sibling or child) or second degree relative (grandparent, uncle or aunt)
    ▪ Family history of myocardial infarction in a first degree relative before the age of 60 or in a second degree relative before the age of 50
    ▪ Total cholesterol greater than 290 mg/dL in an adult first or second degree relative
    ▪ Total cholesterol greater than 260 mg/dL in a child, brother, or sister aged younger than 16 years

• Dutch Lipid Clinic Network Criteria for FH
  o Total score > 5 points

VI. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

KYPROLIS (carfilzomib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Kyprolis is indicated in combination with dexamethasone or with lenalidomide plus dexamethasone for the treatment of patients with relapsed or refractory multiple myeloma who have received one to three lines of therapy.

2. Kyprolis is indicated as a single agent for the treatment of patients with relapsed or refractory multiple myeloma who have received one or more lines of therapy.

B. Compendial Uses

Waldenström macroglobulinemia/lymphoplasmacytic lymphoma

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Multiple Myeloma

Authorization of 12 months may be granted for treatment of multiple myeloma.

B. Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma

Authorization of 12 months may be granted for treatment of Waldenström macroglobulinemia/lymphoplasmacytic lymphoma.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

LARTRUVO (olaratumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Lartruvo is indicated, in combination with doxorubicin, for the treatment of adult patients with soft tissue sarcoma (STS) with a histologic subtype for which an anthracycline-containing regimen is appropriate and which is not amenable to curative treatment with radiotherapy or surgery.

This indication is approved under accelerated approval. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trial.

B. Compendial Use

Lartruvo is indicated, in combination with doxorubicin, for the treatment of adult patients with uterine sarcoma.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Soft Tissue Sarcoma

Authorization of 12 months may be granted for treatment of soft tissue sarcoma (STS) when Lartruvo is used in combination with doxorubicin.

B. Uterine Sarcoma

Authorization of 12 months may be granted for the treatment of uterine sarcoma when Lartruvo is used in combination with doxorubicin.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

LEMTRADA (alemtuzumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Lemtrada is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of Lemtrada should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.

All other indications are considered experimental/investigational and are not covered benefits.

II. CRITERIA FOR APPROVAL

A. First Course – Relapsing forms of multiple sclerosis

Authorization of 30 days (5 doses) may be granted to members with a diagnosis of a relapsing form of multiple sclerosis who have had an inadequate response to two or more drugs indicated for multiple sclerosis.

B. Subsequent Courses – Relapsing forms of multiple sclerosis

Authorization of 30 days (3 doses) may be granted to members with a diagnosis of a relapsing form of multiple sclerosis who have completed at least one previous course of therapy.

III. OTHER CRITERIA

Members will not use Lemtrada concomitantly with other medications used for the treatment of multiple sclerosis, excluding Ampyra.

For subsequent courses, members must have received the previous course of Lemtrada treatment at least 12 months prior to the planned date of the first dose of Lemtrada course of treatment.

IV. REFERENCE

SPECIALTY GUIDELINE MANAGEMENT

LENVIMA (lenvatinib)

POLICY

I. INDICATIONS
The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Lenvima is indicated for the treatment of patients with locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer (DTC).
2. Lenvima is indicated in combination with everolimus, for the treatment of patients with advanced renal cell carcinoma (RCC) following one prior anti-angiogenic therapy.
3. Lenvima is indicated for the first-line treatment of patients with unresectable hepatocellular carcinoma (HCC).

B. Compendial Uses
Medullary, follicular, Hurthle cell or papillary thyroid carcinoma

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Thyroid carcinoma
Authorization of 12 months may be granted for the treatment of medullary, follicular, Hurthle cell, or papillary thyroid carcinoma

B. Renal Cell Carcinoma
Authorization of 12 months may be granted for the treatment of relapsed or advanced renal cell carcinoma.

C. Hepatocellular Carcinoma
Authorization of 12 months may be granted for the treatment of unresectable hepatocellular carcinoma.

III. CONTINUATION OF THERAPY
All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

LEUKINE (sargramostim)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Use Following Induction Chemotherapy in Acute Myelogenous Leukemia
   a. Leukine is indicated for use following induction chemotherapy in older adult patients with acute myelogenous leukemia to shorten time to neutrophil recovery and to reduce the incidence of severe and life-threatening infections and infections resulting in death.

2. Use in Mobilization and Following Transplantation of Autologous Peripheral Blood Progenitor Cells
   a. Leukine is indicated for the mobilization of hematopoietic progenitor cells into peripheral blood for collection by leukapheresis. Mobilization allows for the collection of increased numbers of progenitor cells capable of engraftment as compared with collection without mobilization. After myeloablative chemotherapy, the transplantation of an increased number of progenitor cells can lead to more rapid engraftment, which may result in a decreased need for supportive care. Myeloid reconstitution is further accelerated by administration of Leukine following peripheral blood progenitor cell transplantation.

3. Use in Myeloid Reconstitution After Autologous Bone Marrow Transplantation
   a. Leukine is indicated for acceleration of myeloid recovery in patients with non-Hodgkin's lymphoma (NHL), acute lymphoblastic leukemia (ALL) and Hodgkin's disease undergoing autologous bone marrow transplantation (BMT).

4. Use in Myeloid Reconstitution After Allogeneic Bone Marrow Transplantation
   a. Leukine is indicated for acceleration of myeloid recovery in patients undergoing allogeneic BMT from HLA-matched related donors.

5. Use in Bone Marrow Transplantation Failure or Engraftment Delay
   a. Leukine is indicated in patients who have undergone allogeneic or autologous BMT in whom engraftment is delayed or has failed.

B. Compendial Uses

1. Prophylaxis and treatment of chemotherapy-induced febrile neutropenia in non-myeloid malignancies
2. Treatment of neutropenia in patients with myelodysplastic syndromes (MDS)
3. AML following consolidation chemotherapy
4. ALL following induction or consolidation chemotherapy
5. Agranulocytosis
6. Aplastic anemia
7. Neutropenia related to HIV/AIDS
8. Stem cell transplantation-related indications

All other indications are considered experimental/investigational and are not a covered benefit.
II. CRITERIA FOR INITIAL APPROVAL

A. Neutropenia in cancer patients receiving myelosuppressive chemotherapy
   Authorization of 6 months may be granted for prevention or treatment of febrile neutropenia when both of the following criteria are met:
   1. Member has a non-myeloid malignancy and has received, is currently receiving, or will be receiving myelosuppressive anti-cancer therapy
   2. Leukine will not be administered less than 24 hours before or after chemotherapy or radiotherapy

B. Other indications
   Authorization of 6 months may be granted for members with any of the following indications:
   1. Agranulocytosis
   2. Aplastic anemia
   3. Neutropenia related to HIV/AIDS
   4. Acute myeloid leukemia
   5. Myelodysplastic syndrome
   6. Stem cell transplantation-related indications

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

leuprolide acetate injection

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Prostate cancer: Leuprolide acetate is indicated in the palliative treatment of advanced prostate cancer.
   2. Central precocious puberty (CPP): Leuprolide acetate is indicated in the treatment of children with central precocious puberty.

B. Compendial Uses
   1. Use as a stimulation test to confirm the diagnosis of CPP
   2. Use in combination with growth hormone for children with growth failure and advancing puberty
   3. Prostate cancer
   4. Inhibition of premature luteinizing hormone (LH) surges in women undergoing assisted reproductive technology
   5. Metastatic androgen receptor positive salivary gland tumors

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Central precocious puberty (CPP)
   1. Authorization up to age 12 may be granted for the treatment of CPP in a female member when all of the following criteria are met:
      a. The diagnosis of CPP has been confirmed by a pubertal response to a gonadotropin releasing hormone (GnRH) agonist test or a pubertal level of a third generation luteinizing hormone (LH) assay.
      b. The assessment of bone age versus chronological age supports the diagnosis of CPP.
      c. The member was less than 8 years of age at the onset of secondary sexual characteristics.
   2. Authorization up to age 13 may be granted for the treatment of CPP in a male member when all of the following criteria are met:
      a. The diagnosis of CPP has been confirmed by a pubertal response to a GnRH agonist test or a pubertal level of a third generation LH assay.
      b. The assessment of bone age versus chronological age supports the diagnosis of CPP.
      c. The member was less than 9 years of age at the onset of secondary sexual characteristics.

B. Stimulation test for CPP diagnosis
   Authorization of one dose may be granted for use as a stimulation test to confirm the diagnosis of CPP.

C. Advancing puberty and growth failure


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Authorization of 12 months may be granted for the treatment of advancing puberty and growth failure in a pediatric member when leuprolide acetate is used in combination with growth hormone.

D. Prostate cancer
Authorization of 12 months may be granted for treatment of prostate cancer.

E. Inhibition of premature luteinizing hormone (LH) surge‡
Authorization of 12 months may be granted for the inhibition of premature LH surge in a member undergoing ovulation induction or assisted reproductive technology (ART).

‡ Specialty Guideline Management coverage review will be bypassed for leuprolide if it is being requested for a procedure that has been approved under a member’s medical benefit plan. Such members will be exempt from the requirements in Section IIIE. A medical authorization number and confirmation of the approved procedure(s) will be required. NOTE: Some plans may opt-out of medical benefit alignment. Members receiving coverage under such plans must meet the requirements in Section IIIE.

F. Salivary gland tumors
Authorization of 12 months may be granted for treatment of metastatic salivary gland tumors when the tumor is androgen receptor positive.

III. CONTINUATION OF THERAPY

A. Central precocious puberty
1. Authorization up to age 12 may be granted for continuation of therapy for CPP in a female member if the member is currently less than 12 years of age.
2. Authorization up to age 13 may be granted for continuation of therapy for CPP in a male member if the member is currently less than 13 years of age.

B. Prostate cancer, stimulation test for CPP diagnosis, advancing puberty and growth failure, inhibition of premature LH surge and salivary gland tumors
All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

FUSILEV (levoleucovorin) powder
KHAPZORY (levoleucovorin) powder
levoleucovorin solution

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Levoleucovorin/Fusilev/Khapzory is indicated for rescue after high-dose methotrexate therapy in osteosarcoma.
2. Levoleucovorin/Fusilev/Khapzory is indicated for diminishing the toxicity and counteracting the effects of impaired methotrexate elimination and of inadvertent overdosage of folic acid antagonists.
3. Fusilev is indicated for use in combination chemotherapy with 5-fluorouracil in the palliative treatment of patients with advanced metastatic colorectal cancer.
4. Khapzory is indicated for use in combination chemotherapy with fluorouracil for treatment of metastatic colorectal cancer.

B. Compendial Uses

2. Used in combination with fluorouracil based regimens for colorectal cancer, gastric adenocarcinoma, esophageal/esophagogastric junction cancer, pancreatic cancer, thymomas/thymic carcinomas, cervical cancer, anal adenocarcinoma, occult primary, mucinous ovarian carcinomas, bladder cancer, and neuroendocrine and adrenal tumors when leucovorin is not an available option.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 3 months may be granted for any of the indications listed below when leucovorin is not an appropriate/available option at this time:

A. Rescue treatment after high-dose methotrexate therapy
B. Treatment of a folate antagonist overdose
C. Combination therapy with fluorouracil based chemotherapy regimens
III. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

LIBTAYO (cemiplimab-rwlc)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Libtayo is indicated for the treatment of patients with metastatic cutaneous squamous cell carcinoma (CSCC) or locally advanced CSCC who are not candidates for curative surgery or curative radiation.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Cutaneous squamous cell carcinoma
Authorization of 12 months may be granted for treatment of cutaneous squamous cell carcinoma when all of the following criteria are met:
A. The disease is metastatic or locally advanced
B. The patient is not a candidate for curative surgery or curative radiation

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

LONSURF (trifluridine and tipiracil)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Lonsurf is indicated for the treatment of adult patients with metastatic colorectal cancer who have been previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF biological therapy, and if RAS wild-type, an anti-EGFR therapy.

Lonsurf is indicated for the treatment of adult patients with metastatic gastric or gastroesophageal junction adenocarcinoma previously treated with at least two prior lines of chemotherapy that included a fluoropyrimidine, a platinum, either a taxane or irinotecan, and if appropriate, HER2/neu-targeted therapy.

B. Compendial Uses

Unresectable advanced or metastatic colorectal cancer that was not previously treated with Lonsurf

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Colorectal cancer (CRC)

Authorization of 12 months may be granted for treatment of unresectable advanced or metastatic colorectal cancer when either of the following criteria are met:

1. Member has progressed on treatment with FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, and irinotecan) regimen.
2. Member has progressed on treatment with Irinotecan- AND oxaliplatin-based regimens.

B. Gastric or Gastroesophageal Junction Adenocarcinoma

Authorization of 12 months may be granted for treatment of metastatic gastric or gastroesophageal junction adenocarcinoma when the following criteria are met:

1. Member has been previously treated with at least two prior lines of chemotherapy that included a fluoropyrimidine, a platinum, and either a taxane or irinotecan.
2. If appropriate, member has been treated with HER2/neu-targeted therapy.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.
IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

LORBRENA (lorlatinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Lorbrena is a kinase inhibitor indicated for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) whose disease has progressed on:

- Crizotinib and at least one other ALK inhibitor for metastatic disease; or
- Alectinib as the first ALK inhibitor therapy for metastatic disease; or
- Ceritinib as the first ALK inhibitor therapy for metastatic disease

This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Non-small cell lung cancer (NSCLC)

Authorization of 12 months may be granted for treatment of metastatic NSCLC when all of the following criteria are met:

A. The disease is anaplastic lymphoma kinase (ALK)-positive
B. The disease has progressed on any of the following therapies for metastatic disease:
   1. Crizotinib and at least one other ALK inhibitor
   2. Alectinib as the first ALK inhibitor therapy
   3. Ceritinib as the first ALK inhibitor therapy

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCE

**PRIOR AUTHORIZATION CRITERIA**

<table>
<thead>
<tr>
<th>BRAND NAME*</th>
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</thead>
<tbody>
<tr>
<td>(generic)</td>
</tr>
<tr>
<td>LOTRONEX</td>
</tr>
<tr>
<td>(alosetron)</td>
</tr>
</tbody>
</table>

**Status:** CVS Caremark Criteria  
**Type:** Initial Prior Authorization  
Ref # 129-A

*Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated.

**FDA-APPROVED INDICATIONS**

Lotronex is indicated only for women with severe diarrhea-predominant irritable bowel syndrome (IBS) who have:
- chronic IBS symptoms (generally lasting six months or longer),
- had anatomic or biochemical abnormalities of the gastrointestinal tract excluded, and
- not responded adequately to conventional therapy

Diarrhea-predominant IBS is severe if it includes diarrhea and one or more of the following:
- frequent and severe abdominal pain/discomfort
- frequent bowel urgency or fecal incontinence
- disability or restriction of daily activities due to IBS

Because of infrequent but serious gastrointestinal adverse events associated with Lotronex, the indication is restricted to those patients for whom the benefit-to-risk balance is most favorable.

Clinical studies have not been performed to adequately confirm the benefits of Lotronex in men.

**COVERAGE CRITERIA**

The requested drug will be covered with prior authorization when the following criteria are met:
- The requested drug is being prescribed for a biological female or a person that self-identifies as a female with a diagnosis of severe diarrhea-predominant irritable bowel syndrome (IBS) AND all of the following apply: A) Chronic IBS symptoms lasting at least 6 months, B) Gastrointestinal tract abnormalities have been ruled out, C) Inadequate response to conventional therapy

**RATIONALE**

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Lotronex is indicated only for women with severe diarrhea-predominant irritable bowel syndrome (IBS) who have: chronic IBS symptoms (generally lasting six months or longer), had anatomic or biochemical abnormalities of the gastrointestinal tract excluded, and not responded adequately to conventional therapy

Diarrhea-predominant IBS is severe if it includes diarrhea and one or more of the following: frequent and severe abdominal pain/discomfort, frequent bowel urgency or fecal incontinence, disability or restriction of daily activities due to IBS.

**REFERENCES**

3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA.

Written by: UM Development (LS)
Date Written: 09/2003
Revised:
(JG) 11/2002; (MG) 08/2003; (CM) 09/2004; (JG) 10/2005; (CT) 06/2006, 05/2007, 06/2008, 06/2009, 06/2010, 07/2011, 07/2012; 10/2012 (extended duration), 08/2013; (JH) 08/2014, 08/2015; (KM) 08/2016 (removed safety question, removed female from question 1), 09/2016 (updated wording of criteria for approval to not discriminate for TGC patients); (DS) 08/2017 (no clinical changes); (JG) 09/2018 (no clinical changes)
Reviewed:

CRITERIA FOR APPROVAL

1. Is the requested drug being prescribed for a biological female or a person that self-identifies as a female with a diagnosis of severe diarrhea-predominant irritable bowel syndrome (IBS) AND do all of the following apply: A) Chronic IBS symptoms lasting at least 6 months, B) Gastrointestinal tract abnormalities have been ruled out, C) Inadequate response to conventional therapy?

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
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</thead>
<tbody>
<tr>
<td><strong>1. Approve, 36 months</strong></td>
<td><strong>Deny</strong></td>
</tr>
</tbody>
</table>

DELEGATION REASONS – DO NOT USE FOR MEDICARE PART D

- You do not meet the requirements of your plan. Your plan covers this drug when you are a biological female or you self-identify as female with severe diarrhea-predominant irritable bowel syndrome (IBS) and all of the following:
  - You have had IBS symptoms for at least 6 months
  - Gastrointestinal tract abnormalities have been ruled out
  - Other therapies did not work for you

Your request has been denied based on the information we have.

[Short Description: No approvable diagnosis]
PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>BRAND NAME*</th>
<th>LOTRONEX</th>
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**Status:** CVS Caremark Criteria  
**Type:** Initial Prior Authorization

Ref# 129-A  
Ref# 690-A

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

**FDA-APPROVED INDICATIONS**

Lotronex is indicated only for women with severe diarrhea-predominant irritable bowel syndrome (IBS) who have:

- chronic IBS symptoms (generally lasting six months or longer),
- had anatomic or biochemical abnormalities of the gastrointestinal tract excluded, and
- not responded adequately to conventional therapy

Diarrhea-predominant IBS is severe if it includes diarrhea and one or more of the following:

- frequent and severe abdominal pain/discomfort
- frequent bowel urgency or fecal incontinence
- disability or restriction of daily activities due to IBS

Because of infrequent but serious gastrointestinal adverse events associated with Lotronex, the indication is restricted to those patients for whom the benefit-to-risk balance is most favorable.

Clinical studies have not been performed to adequately confirm the benefits of Lotronex in men.

**COVERAGE CRITERIA**

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for a biological female or a person that self-identifies as a female with a diagnosis of severe diarrhea-predominant irritable bowel syndrome (IBS)
- The patient has experienced chronic irritable bowel syndrome (IBS) symptoms lasting at least 6 months
- Gastrointestinal tract abnormalities have been ruled out
- The patient has had an inadequate response to conventional therapy

**RATIONALE**

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Lotronex is indicated only for women with severe diarrhea-predominant irritable bowel syndrome (IBS) who have: chronic IBS symptoms (generally lasting six months or longer), had anatomic or biochemical abnormalities of the gastrointestinal tract excluded, and not responded adequately to conventional therapy.

Because of infrequent but serious gastrointestinal adverse events associated with Lotronex, the indication is restricted to those patients for whom the benefit-to-risk balance is most favorable. Clinical studies have not been performed to adequately confirm the benefits of Lotronex in men.
1. Is the requested drug being prescribed for a biological female or a person that self-identifies as a female with a diagnosis of severe diarrhea-predominant irritable bowel syndrome (IBS)?

   Yes  No

2. Has the patient experienced chronic irritable bowel syndrome (IBS) symptoms lasting at least 6 months?

   Yes  No

3. Have gastrointestinal tract abnormalities been ruled out?

   Yes  No

4. Has the patient had an inadequate response to conventional therapy?

   Yes  No

Mapping Instructions (129-A)

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
<th>DENIAL REASONS – DO NOT USE FOR MEDICARE PART D</th>
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<tbody>
<tr>
<td>1. Go to 2</td>
<td>Deny</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you are a biological female or you self-identify as female with severe diarrhea-predominant irritable bowel syndrome (IBS). Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]</td>
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<tr>
<td>2. Go to 3</td>
<td>Deny</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have had IBS symptoms for at least 6 months. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]</td>
</tr>
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<td>3. Go to 4</td>
<td>Deny</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have had gastrointestinal tract abnormalities ruled out. Your request has been denied based on the information we have.</td>
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<tr>
<td>4.</td>
<td>Approve, 36 months</td>
<td>Deny</td>
</tr>
<tr>
<td></td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when other therapies did not work for you.</td>
<td>Your request has been denied based on the information we have.</td>
</tr>
<tr>
<td></td>
<td>[Short Description: No approvable diagnosis]</td>
<td></td>
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</table>

### Mapping Instructions (690-A)

<table>
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<tr>
<th></th>
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<tbody>
<tr>
<td>1.</td>
<td>Go to 2</td>
<td>Deny</td>
</tr>
<tr>
<td></td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you are a biological female or you self-identify as female with severe diarrhea-predominant irritable bowel syndrome (IBS).</td>
<td>Your request has been denied based on the information we have.</td>
</tr>
<tr>
<td></td>
<td>[Short Description: No approvable diagnosis]</td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>Go to 3</td>
<td>Deny</td>
</tr>
<tr>
<td></td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have had IBS symptoms for at least 6 months.</td>
<td>Your request has been denied based on the information we have.</td>
</tr>
<tr>
<td></td>
<td>[Short Description: No approvable diagnosis]</td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>Go to 4</td>
<td>Deny</td>
</tr>
<tr>
<td></td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have had gastrointestinal tract abnormalities ruled out.</td>
<td>Your request has been denied based on the information we have.</td>
</tr>
<tr>
<td></td>
<td>[Short Description: No approvable diagnosis]</td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>Approve, 12 months</td>
<td>Deny</td>
</tr>
<tr>
<td></td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when other therapies did not work for you.</td>
<td>Your request has been denied based on the information we have.</td>
</tr>
<tr>
<td></td>
<td>[Short Description: No approvable diagnosis]</td>
<td></td>
</tr>
</tbody>
</table>
POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
A. Neovascular (wet) age-related macular degeneration
B. Macular edema following retinal vein occlusion
C. Diabetic macular edema
D. Diabetic retinopathy
E. Myopic choroidal neovascularization

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Diabetic Macular Edema
   Authorization of 24 months may be granted for treatment of diabetic macular edema.

B. Neovascular (Wet) Age-Related Macular Degeneration
   Authorization of 24 months may be granted for treatment of neovascular (wet) age-related macular degeneration.

C. Macular Edema Following Retinal Vein Occlusion
   Authorization of 24 months may be granted for treatment of macular edema following retinal vein occlusion.

D. Diabetic Retinopathy
   Authorization of 24 months may be granted for treatment of diabetic retinopathy.

E. Myopic Choroidal Neovascularization
   Authorization of 24 months may be granted for treatment of myopic choroidal neovascularization.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.
IV. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

LUMIZYME (alglucosidase alfa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Lumizyme is indicated for patients with Pompe disease (acid alpha-glucosidase [GAA] deficiency).

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Pompe disease
Indefinite authorization may be granted for treatment of Pompe disease when the diagnosis of Pompe disease was confirmed by enzyme assay demonstrating a deficiency of acid alpha-glucosidase enzyme activity or by genetic testing.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

LUMOXITI (moxetumomab pasudotox-tdfk)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Lumoxiti is a CD22-directed cytotoxin indicated for the treatment of adult patients with relapsed or refractory hairy cell leukemia (HCL) who received at least two prior systemic therapies, including treatment with a purine nucleoside analog (PNA).

Limitations of use

Lumoxiti is not recommended in patients with severe renal impairment (CrCl ≤ 29 mL/min).

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Hairy Cell Leukemia

Authorization of 6 months may be granted for treatment of relapsed or refractory hairy cell leukemia when all of the following criteria are met:

A. The patient has received at least two prior systemic therapies, including treatment with a purine nucleoside analog.
B. The patient has not previously received 6 or more cycles of treatment with Lumoxiti.

III. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

LUPANETA PACK-1 Month 3.75 mg
LUPANETA PACK-3 Month 11.25 mg
(leuprolide acetate for depot suspension/norethindrone acetate)

POLICY

I. INDICATIONS
   The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

   **FDA-Approved Indication**
   Lupaneta Pack is indicated for initial management of the painful symptoms of endometriosis and for management of recurrence of symptoms.

   Limitations of Use: Duration of use is limited due to concerns about adverse impact on bone mineral density. The initial treatment course of Lupaneta Pack is limited to six months. A single retreatment course of not more than six months may be administered after the initial course of treatment if symptoms recur. Use of Lupaneta Pack for longer than a total of 12 months is not recommended.

   All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL
   **Endometriosis**
   Authorization of up to 6 months (one treatment course) may be granted to members for initial treatment of endometriosis.

III. CONTINUATION OF THERAPY
   **Endometriosis**
   Authorization of up to 6 months (for a lifetime maximum of 12 months total) may be granted for retreatment of endometriosis when all of the following criteria are met:
   A. The member has had a recurrence of symptoms
   B. The member has a bone mineral density within normal limits

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

LUPRON DEPOT 3.75 mg
LUPRON DEPOT-3 Month 11.25 mg
(leuprolide acetate for depot suspension)

POLICY

I. INDICATIONS
The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Lupron Depot 3.75 mg and Lupron Depot-3 Month 11.25 mg are indicated for management of endometriosis, including pain relief and reduction of endometriotic lesions. Lupron Depot 3.75 mg monthly and Lupron Depot-3 Month 11.25 mg with norethindrone acetate 5 mg daily are also indicated for initial management of endometriosis and for management of recurrence of symptoms. Duration of initial treatment or retreatment should be limited to six months.

2. When used concomitantly with iron therapy, Lupron Depot 3.75 mg and Lupron Depot-3 Month 11.25 mg are indicated for the preoperative hematologic improvement of patients with anemia caused by uterine leiomyomata. The clinician may wish to consider a one-month trial period on iron alone inasmuch as some of the patients will respond to iron alone. Lupron may be added if the response to iron alone is considered inadequate. Recommended duration of therapy is up to 3 months, either given as Lupron Depot 3.75 mg monthly or as a single injection of Lupron Depot-3 Month 11.25 mg. Lupron Depot-3 Month 11.25 mg is indicated only for women for whom three months of hormonal suppression is deemed necessary.

Experience with Lupron Depot in females has been limited to women 18 years of age and older, and experience with the Lupron Depot-3 Month 11.25 mg formulation has been limited to treatment for no more than six months.

B. Compendial Uses
1. Breast cancer
2. Ovarian Cancer
   a. Epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer
   b. Malignant sex cord-stromal tumors
3. Preoperative use in uterine leiomyomata (fibroids) to facilitate surgery
4. Gender dysphoria (also known as gender non-conforming or transgender persons)
   NOTE: Some plans may opt-out of coverage for gender dysphoria.
5. Preservation of ovarian function
6. Prevention of recurrent menstrual related attacks in acute porphyria

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL
A. **Endometriosis**  
Authorization of up to 6 months (one treatment course) may be granted to members for initial treatment of endometriosis.

B. **Uterine leiomyomata (fibroids)**  
Authorization of up to 3 months may be granted for initial treatment of uterine leiomyomata (fibroids) when either of the following criteria is met:
1. Member has anemia due to uterine leiomyomata, or
2. Lupron Depot will be used prior to surgery for uterine leiomyomata.

C. **Breast cancer**  
Authorization of 12 months may be granted for treatment of hormone receptor-positive breast cancer.

D. **Ovarian cancer**
1. Authorization of 12 months may be granted for treatment of epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer.
2. Authorization of 12 months may be granted for treatment of malignant sex cord-stromal tumors.

E. **Gender dysphoria**
1. Authorization of 12 months may be granted for pubertal suppression in preparation for gender reassignment in an adolescent member when all of the following criteria are met:
   a. The member has a diagnosis of gender dysphoria.
   b. The member has reached Tanner stage 2 of puberty.
2. Authorization of 12 months may be granted for gender reassignment in an adult member when all of the following criteria are met:
   a. The member has a diagnosis of gender dysphoria.
   b. The member will receive Lupron Depot concomitantly with cross sex hormones.

F. **Preservation of ovarian function**
Authorization of 3 months may be granted for preservation of ovarian function when the member is premenopausal and undergoing chemotherapy.

G. **Prevention of recurrent menstrual related attacks in acute porphyria**
Authorization of 12 months may be granted for prevention of recurrent menstrual related attacks in members with acute porphyria when the requested medication is prescribed by or in consultation with a physician experienced in the management of porphyrias.

III. **CONTINUATION OF THERAPY**
All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria in addition to the following diagnosis-specific criteria (if applicable).

A. **Endometriosis**
Authorization of up to 6 months (for a lifetime maximum of 12 months total) may be granted for retreatment of endometriosis when all of the following criteria are met:
1. The member has had a recurrence of symptoms.
2. The member has a bone mineral density within normal limits.

B. **Uterine leiomyomata (fibroids)**
Authorization of up to 3 months (for a lifetime maximum of 6 months total) may be granted when either of the following criteria is met:
1. Member has anemia due to uterine leiomyomata, or
2. Lupron Depot will be used prior to surgery for uterine leiomyomata.

C. All other indications
All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

LUPRON DEPOT 1-Month 7.5 mg
LUPRON DEPOT 3-Month 22.5 mg
LUPRON DEPOT 4-Month 30 mg
LUPRON DEPOT 6-Month 45 mg
(leuprolide acetate for depot suspension)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Lupron Depot 7.5 mg, Lupron Depot 3-Month 22.5 mg, Lupron Depot 4-Month 30 mg, and Lupron Depot 6-Month 45 mg are indicated in the palliative treatment of advanced prostate cancer.

B. Compendial Uses
1. Prostate cancer
2. Metastatic androgen receptor positive salivary gland tumor
3. Gender dysphoria (also known as gender non-conforming or transgender persons)
   
   NOTE: Some plans may opt-out of coverage for gender dysphoria.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Prostate cancer
Authorization of 12 months may be granted for treatment of prostate cancer.

B. Gender dysphoria
1. Authorization of 12 months may be granted for pubertal suppression in preparation for gender reassignment in an adolescent member when all of the following criteria are met:
   a. The member has a diagnosis of gender dysphoria.
   b. The member has reached Tanner stage 2 of puberty.
2. Authorization of 12 months may be granted for gender reassignment in an adult member when all of the following criteria are met:
   a. The member has a diagnosis of gender dysphoria.
   b. The member will receive Lupron Depot concomitantly with cross sex hormones.

C. Salivary gland tumor
Authorization of 12 months may be granted for treatment of metastatic salivary gland tumors when the tumor is androgen receptor positive.
III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Lupron Depot 7.5 mg, 22.5, 30mg, 45mg [package insert]. North Chicago, IL: AbbVie Inc.; December 2018.
SPECIALTY GUIDELINE MANAGEMENT

Lupron Depot-PED (leuprolide acetate for depot suspension)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Lupron Depot-PED is indicated for the treatment of children with central precocious puberty (CPP).

B. Compendial Use
Gender dysphoria (also known as gender non-conforming or transgender persons)

NOTE: Some plans may opt-out of coverage for gender dysphoria.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Central precocious puberty (CPP)

1. Authorization up to age 12 may be granted for the treatment of CPP in a female member when all of the following criteria are met:
   a. The diagnosis of CPP has been confirmed by a pubertal response to a gonadotropin releasing hormone (GnRH) agonist test or a pubertal level of a third generation luteinizing hormone (LH) assay.
   b. The assessment of bone age versus chronological age supports the diagnosis of CPP.
   c. The member was less than 8 years of age at the onset of secondary sexual characteristics.

2. Authorization up to age 13 may be granted for the treatment of CPP in a male member when all of the following criteria are met:
   a. The diagnosis of CPP has been confirmed by a pubertal response to a GnRH agonist test or a pubertal level of a third generation LH assay.
   b. The assessment of bone age versus chronological age supports the diagnosis of CPP.
   c. The member was less than 9 years of age at the onset of secondary sexual characteristics.

B. Gender dysphoria

1. Authorization of 12 months may be granted for pubertal suppression in preparation for gender reassignment in an adolescent member when all of the following criteria are met:
   a. The member has a diagnosis of gender dysphoria.
   b. The member has reached Tanner stage 2 of puberty.

2. Authorization of 12 months may be granted for gender reassignment in an adult member when all of the following criteria are met:
   a. The member has a diagnosis of gender dysphoria.
   b. The member will receive Lupron Depot-PED concomitantly with cross sex hormones.
III. CONTINUATION OF THERAPY

A. Central precocious puberty (CPP)
   1. Authorization up to age 12 may be granted for continuation of therapy for CPP in a female member if the member is currently less than 12 years of age.
   2. Authorization up to age 13 may be granted for continuation of therapy for CPP in a male member if the member is currently less than 13 years of age.

B. Gender Dysphoria
   All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

LUTATHERA (lutetium Lu 177 dotatate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut, and hindgut neuroendocrine tumors in adults.

All other indications are considered experimental/investigational and are not a covered benefit.

Compendial uses

- Neuroendocrine tumors (NETs) of the lung and thymus (carcinoid tumors)
- Pheochromocytoma/paraganglioma

II. CRITERIA FOR INITIAL APPROVAL

A. Gastroenteropancreatic neuroendocrine tumors (GEP-NETs)

Authorization of 12 months may be granted for treatment of somatostatin receptor-positive GEP-NETs.

B. Neuroendocrine tumors (NETs) of the lung and thymus (carcinoid tumors)

Authorization of 12 months may be granted for treatment of somatostatin receptor-positive NETs of the lung and thymus (carcinoid tumors)

C. Pheochromocytoma/paraganglioma

Authorization of 12 months may be granted for treatment of somatostatin receptor-positive pheochromocytoma/paraganglioma

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCE

SPECIALTY GUIDELINE MANAGEMENT

LUXTURNA (voretigene neparvovec-rzyl)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Luxturna is indicated for the treatment of patients with confirmed biallelic RPE65 mutation-associated retinal dystrophy. Patients must have viable retinal cells as determined by the treating physician(s).

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED INFORMATION

Testing or analysis confirming a genetic diagnosis of biallelic RPE65 gene mutations.

III. CRITERIA FOR INITIAL APPROVAL

Biallelic RPE65 mutation-associated retinal dystrophy
Authorization of 1 month may be granted for treatment of biallelic RPE65 mutation-associated retinal dystrophy when all of the following criteria are met:

A. The member has not received a previous treatment course of Luxturna.
B. The member has viable retinal cells in both eyes as determined by retinal thickness on spectral domain optical coherence tomography, fundus photography, and clinical examination.
C. The member must have either of the following in both eyes:
   1. Visual acuity of 20/60 or worse.
   2. Visual field less than 20 degrees in any meridian.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

LYNPARZA (olaparib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Ovarian Cancer

1. First-Line Maintenance Treatment of BRCA-mutated Advanced Ovarian Cancer
   Lynparza is indicated for the maintenance treatment of adult patients with deleterious or suspected deleterious germline or somatic BRCA-mutated (gBRCAm or sBRCAm) advanced epithelial ovarian, fallopian tube or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy.

2. Maintenance Treatment of Recurrent Ovarian Cancer
   Lynparza is indicated for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer, who are in complete or partial response to platinum-based chemotherapy.

3. Advanced gBRCA-mutated Ovarian Cancer After 3 or More Lines of Chemotherapy
   Lynparza is indicated for the treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy.

B. Breast Cancer

Germline BRCA-mutated HER2-negative metastatic breast cancer
Lynparza is indicated in patients with deleterious or suspected deleterious gBRCAm, HER2-negative metastatic breast cancer, who have been treated with chemotherapy in the neoadjuvant, adjuvant, or metastatic setting. Patients with hormone receptor (HR)-positive breast cancer should have been treated with a prior endocrine therapy or be considered inappropriate for endocrine therapy.

Compendial uses

Breast cancer
Recurrent or metastatic HER2-negative, BRCA 1/2-germline mutated breast cancer that is hormone receptor-negative or hormone receptor-positive and endocrine therapy refractory

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Ovarian Cancer

Authorization of 12 months may be granted for the treatment of advanced or recurrent ovarian cancer when the member has received prior treatment with chemotherapy.

B. Breast Cancer

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Authorization of 12 months may be granted for the treatment of human epidermal growth factor receptor 2 (HER2)-negative recurrent or metastatic breast cancer in members with deleterious or suspected deleterious germline BRCA mutations.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

MAVENCLAD (cladribine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Mavenclad is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include relapsing-remitting disease and active secondary progressive disease, in adults. Because of its safety profile, use of Mavenclad is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternative drug indicated for the treatment of MS.

Limitations of Use

Mavenclad is not recommended for use in patients with clinically isolated syndrome (CIS) because of its safety profile.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Multiple Sclerosis

A. Initial requests

Authorization of 45 days may be granted for treatment of relapsing forms of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapses) and when all of the following criteria are met:

1. Inadequate response or unable to tolerate an alternative drug indicated for the treatment of multiple sclerosis.
2. Member does not have clinically isolated syndrome (CIS).
3. Member has not received 2 courses (i.e., 4 cycles) of Mavenclad.
4. Members will not use Mavenclad concomitantly with other medications used for the treatment of multiple sclerosis, excluding Ampyra.

B. Subsequent requests

Authorization of 45 days may be granted for treatment of relapsing forms of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapses) and when all of the following criteria are met:

1. Member has not received 2 courses (i.e., 4 cycles) of Mavenclad.
2. Members will not use Mavenclad concomitantly with other medications used for the treatment of multiple sclerosis, excluding Ampyra.
3. The member has not received Mavenclad in the last 43 weeks.

III. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

MAVYRET (glecaprevir and pibrentasvir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Mavyret is indicated for the treatment of adult patients with chronic hepatitis C virus (HCV) genotype (GT) 1, 2, 3, 4, 5 or 6 infection without cirrhosis or with compensated cirrhosis (Child-Pugh A). Mavyret is also indicated for the treatment of adult patients with HCV genotype 1 infection, who previously have been treated with a regimen containing an HCV NS5A inhibitor or an NS3/4A protease inhibitor (PI), but not both.

All other indications are considered experimental/investigational and are not a covered benefit.

II. EXCLUSIONS

Coverage will not be provided for members with decompensated cirrhosis/moderate or severe hepatic impairment (Child Turcotte Pugh Class B or C)

Note: When the requested drug is being used in a combination therapy regimen, exclusions to the other antiviral drugs also apply.

III. CRITERIA FOR INITIAL APPROVAL

A. Chronic hepatitis C virus infection
   1. Genotype 1 infection
      a. Authorization of up to 8 weeks total may be granted for treatment-naive members without cirrhosis.
      b. Authorization of up to 12 weeks total may be granted for treatment-naive members with compensated cirrhosis.
      c. Authorization of up to 16 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with an NS5A inhibitor and who have not received an NS3/4A protease inhibitor.
      d. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with an NS3/4A protease inhibitor (e.g., simeprevir, boceprevir or telaprevir in combination with peginterferon and ribavirin, simeprevir with sofosbuvir) and who have not received an NS5A inhibitor.
      e. Authorization of up to 8 weeks total may be granted for members without cirrhosis who failed prior treatment with peginterferon-alfa (PEG-IFN) and ribavirin (RBV) and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
f. Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.

g. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with a sofosbuvir (Sovaldi)-containing regimen (e.g., sofosbuvir and ribavirin with or without PEG-IFN) and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.

2. **Genotype 2 infection**
   a. Authorization of up to 8 weeks total may be granted for treatment-naive members without cirrhosis.
   b. Authorization of up to 12 weeks total may be granted for treatment-naive members with compensated cirrhosis.
   c. Authorization of up to 8 weeks total may be granted for members without cirrhosis who failed prior treatment with PEG-IFN and RBV and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
   d. Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
   e. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with sofosbuvir (Sovaldi) and ribavirin with or without PEG-IFN and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.

3. **Genotype 3 infection**
   a. Authorization of up to 8 weeks total may be granted for treatment-naive members without cirrhosis.
   b. Authorization of up to 12 weeks total may be granted for treatment-naive members with compensated cirrhosis.
   c. Authorization of up to 16 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
   d. Authorization of up to 16 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with sofosbuvir (Sovaldi) and RBV with or without PEG-IFN and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.

4. **Genotype 4, 5, or 6 infection**
   a. Authorization of up to 8 weeks total may be granted for treatment-naive members without cirrhosis.
   b. Authorization of up to 12 weeks total may be granted for treatment-naive members with compensated cirrhosis.
   c. Authorization of up to 8 weeks total may be granted for members without cirrhosis who failed prior treatment with PEG-IFN and RBV and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
   d. Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
   e. Authorization of up to 8 weeks total may be granted for members without cirrhosis who failed prior treatment with sofosbuvir (Sovaldi) and ribavirin with or without PEG-IFN and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
   f. Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with sofosbuvir (Sovaldi) and ribavirin with or without PEG-IFN and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
5. Recurrent HCV infection post liver transplantation
   a. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis and recurrent HCV genotype 1, 2, 3, 4, 5 or 6 infection post liver transplantation.
   b. Authorization of up to 16 weeks total may be granted for members with recurrent HCV genotype 1 infection post liver transplantation without cirrhosis or with compensated cirrhosis who failed prior treatment with an NS5A inhibitor and who have not received an NS3/4A protease inhibitor.
   c. Authorization of up to 16 weeks total may be granted for members with recurrent HCV genotype 3 infection post liver transplantation without cirrhosis or with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
   d. Authorization of up to 16 weeks total may be granted for members with HCV recurrent genotype 3 infection post liver transplantation without cirrhosis or with compensated cirrhosis who failed prior treatment with sofosbuvir (Sovaldi) and RBV with or without PEG-IFN and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.

6. Kidney transplant recipients
   a. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have HCV genotype 1, 2, 3, 4, 5 or 6 infection.
   b. Authorization of up to 16 weeks total may be granted for members with HCV genotype 1 infection without cirrhosis or with compensated cirrhosis who failed prior treatment with an NS5A inhibitor and who have not received an NS3/4A protease inhibitor.
   c. Authorization of up to 16 weeks total may be granted for members with HCV genotype 3 infection without cirrhosis or with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
   d. Authorization of up to 16 weeks total may be granted for members with HCV genotype 3 infection without cirrhosis or with compensated cirrhosis who failed prior treatment with sofosbuvir (Sovaldi) and RBV with or without PEG-IFN and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.

B. HCV and HIV Coinfection
   Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A above are met.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

MAYZENT (siponimod)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Mayzent is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease and active secondary progressive disease, in adults.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Relapsing forms of multiple sclerosis
Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

B. Clinically isolated syndrome
Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome.

III. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted for members who are experiencing disease stability or improvement while receiving Mayzent.

IV. OTHER CRITERIA

Members will not use Mayzent concomitantly with other medications used for the treatment of multiple sclerosis, excluding Ampyra.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

MEKINIST (trametinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Mekinist is indicated, as a single agent or in combination with dabrafenib, for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test.
   2. Mekinist is indicated, in combination with dabrafenib, for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation as detected by an FDA-approved test.
   3. Mekinist is indicated, in combination with dabrafenib, for the adjuvant treatment of patients with melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test, and involvement of lymph node(s), following complete resection.
   4. Mekinist is indicated, in combination with dabrafenib, for the treatment of patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) with BRAF V600E mutation and no satisfactory locoregional treatment options.

B. Compendial Uses
   1. Melanoma (including brain metastases), BRAF V600 activating mutation-positive
   2. Glioma, BRAF V600 activating mutation-positive
   3. Meningioma, BRAF V600 activating mutation-positive
   4. Astrocytoma, BRAF V600 activating mutation-positive
   5. Uveal melanoma as a single agent
   6. Colorectal cancer, BRAF V600E activating mutation-positive

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of BRAF mutation documentation is necessary to initiate the prior authorization review for applicable indications as outlined in section III.

III. CRITERIA FOR INITIAL APPROVAL

A. Melanoma
   1. Authorization of 12 months may be granted for treatment of unresectable or metastatic cutaneous melanoma with a BRAF V600 activating mutation as a single agent or in combination with dabrafenib (Tafinlar).
   2. Authorization of 12 months may be granted for treatment of brain metastases from melanoma with a BRAF V600 activating mutation in combination with dabrafenib (Tafinlar).
3. Authorization of 12 months may be granted for adjuvant treatment of cutaneous melanoma with a BRAF V600 activating mutation in combination with dabrafenib (Tafinlar).
4. Authorization of 12 months may be granted for treatment of metastatic or unresectable uveal melanoma as a single agent.

B. Non-Small Cell Lung Cancer (NSCLC)
Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive NSCLC in combination with dabrafenib (Tafinlar).

C. Anaplastic Thyroid Cancer (ATC)
Authorization of 12 months may be granted for treatment of metastatic BRAF V600E mutation-positive ATC in combination with dabrafenib (Tafinlar).

D. Central Nervous System Cancer
Authorization of 12 months may be granted for treatment of BRAF V600 mutation-positive gliomas, meningiomas, or astrocytomas.

E. Colorectal Cancer
Authorization of 12 months may be granted for treatment of unresectable advanced or metastatic colorectal cancer when the following criteria are met:
1. Mekinist is used in combination with dabrafenib (Tafinlar) and either cetuximab or panitumumab
2. Tumor is positive for BRAF V600E mutation.
3. Will be used as subsequent therapy

IV. CONTINUATION OF THERAPY
Authorization of 12 months may be granted for continuation of therapy for an indication outlined in section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen. For patients using Mekinist for adjuvant treatment of cutaneous melanoma, only 12 months of therapy total will be approved.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

MEKTOVI (binimetinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Mektovi is indicated, in combination with encorafenib, for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, as detected by an FDA-approved test.

B. Compendial Uses

1. Glioma, BRAF V600 activating mutation-positive
2. Meningioma, BRAF V600 activating mutation-positive
3. Astrocytoma, BRAF V600 activating mutation-positive
4. Colorectal cancer, BRAF V600E activating mutation-positive

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of BRAF mutation documentation is necessary to initiate the prior authorization review.

III. CRITERIA FOR INITIAL APPROVAL

A. Melanoma

Authorization of 12 months may be granted for treatment of unresectable or metastatic melanoma when all of the following criteria are met:
1. Mektovi is used in combination with encorafenib (Braftovi)
2. Tumor is positive for BRAF V600E or V600K mutation.

B. Central Nervous System Cancer

Authorization of 12 months may be granted for treatment of BRAF V600 mutation-positive gliomas, meningiomas, or astrocytomas.

C. Colorectal Cancer

Authorization of 12 months may be granted for treatment of unresectable advanced or metastatic colorectal cancer when the following criteria are met:
1. Mektovi is used in combination with encorafenib (Braftovi) and either cetuximab or panitumumab
2. Tumor is positive for BRAF V600E mutation.
3. Will be used as subsequent therapy
IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

MENOPUR (menotropins for injection)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Menopur is indicated for development of multiple follicles and pregnancy in ovulatory women as part of an assisted reproductive technology (ART) cycle.

All other indications are considered experimental/investigational and are not a covered benefit.

II. MEDICAL BENEFIT ALIGNMENT

Specialty Guideline Management coverage review will be bypassed for drug(s) being requested for a procedure that has been approved under a member’s medical benefit plan. Such members will be exempt from the requirements in Sections III and IV. A medical authorization number and confirmation of the approved procedure(s) will be required.

NOTE: Some plans may opt-out of medical benefit alignment. Members receiving coverage under such plans must meet the requirements in Sections III and IV.

III. CRITERIA FOR INITIAL APPROVAL

Follicle stimulation
Authorization of 12 months may be granted for members undergoing ovulation induction or assisted reproductive technology who meet any of the following criteria:
1. Member has completed three or more previous cycles of clomiphene, or
2. Member has a risk factor for poor ovarian response to clomiphene, or
3. Member has a contraindication or exclusion to clomiphene, or
4. Member is 37 years of age or older

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

 MEPSEVII (vestronidase alfa-vjbk)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Mepsevii is indicated in pediatric and adult patients for the treatment of Mucopolysaccharidosis VII (MPS VII, Sly syndrome).

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Mucopolysaccharidosis VII (MPS VII, Sly syndrome)
Indefinite authorization may be granted for treatment of MPS VII (Sly syndrome) when the diagnosis of MPS VII was confirmed by enzyme assay demonstrating a deficiency of beta-glucuronidase enzyme activity or by genetic testing.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

QUANTITY LIMIT CRITERIA

<table>
<thead>
<tr>
<th>BRAND NAME*</th>
</tr>
</thead>
<tbody>
<tr>
<td>METHADOSE 10 MG/ML**</td>
</tr>
<tr>
<td>(methadone oral concentrate)</td>
</tr>
<tr>
<td>METHADOSE 40 MG DISPERSIBLE TABLET**</td>
</tr>
<tr>
<td>(methadone dispersible tablets)</td>
</tr>
</tbody>
</table>

Status: CVS Caremark Criteria  
Type: Quantity Limit  
Ref# 1357-H

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

**Please note that these methadone products are indicated for detoxification/opioid addiction ONLY. Methadone products indicated for BOTH detoxification/opioid addiction AND pain are targeted on the Opioids ER criteria.

FDA-APPROVED INDICATIONS

Methadone Concentrate
1. For detoxification treatment of opioid addiction (heroin or other morphine-like drugs).
2. For maintenance treatment of opioid addiction (heroin or other morphine-like drugs), in conjunction with appropriate social and medical services.

Methadone Dispersible
Methadone hydrochloride tablets for oral suspension contain methadone, an opioid agonist indicated for the:
- Detoxification treatment of opioid addiction (heroin or other morphine-like drugs).
- Maintenance treatment of opioid addiction (heroin or other morphine-like drugs), in conjunction with appropriate social and medical services.

Conditions For Distribution And Use Of Methadone Products For The Treatment Of Opioid Addiction

Code of Federal Regulations, Title 42, Sec 8: Methadone products, when used for the treatment of opioid addiction in detoxification or maintenance programs, shall be dispensed only by opioid treatment programs (and agencies, practitioners or institutions by formal agreement with the program sponsor) certified by the Substance Abuse and Mental Health Services Administration and approved by the designated state authority. Certified treatment programs shall dispense and use methadone in oral form only and according to the treatment requirements stipulated in the Federal Opioid Treatment Standards (42 CFR 8.12). See below for important regulatory exceptions to the general requirement for certification to provide opioid agonist treatment.

Failure to abide by the requirements in these regulations may result in criminal prosecution, seizure of the drug supply, revocation of the program approval, and injunction precluding operation of the program.

Regulatory Exceptions To The General Requirement For Certification To Provide Opioid Agonist Treatment:
- During inpatient care, when the patient was admitted for any condition other than concurrent opioid addiction [pursuant to 21 CFR 1306.07(c)], to facilitate the treatment of the primary admitting diagnosis.
- During an emergency period of no longer than 3 days while definitive care for the addiction is being sought in an appropriately licensed facility [pursuant to 21 CFR 1306.07(b)].
RATIONALE

Methadone oral solution concentrate and dispersible tablets are indicated for detoxification treatment of opioid addiction (heroin or other morphine-like drugs) and maintenance treatment of opioid addiction (heroin or other morphine-like drugs), in conjunction with appropriate social and medical services.¹⁻⁴

Methadone products, when used for the treatment of opioid addiction in detoxification or maintenance programs, shall be dispensed only by opioid treatment programs (and agencies, practitioners or institutions by formal agreement with the program sponsor) certified by the Substance Abuse and Mental Health Services Administration and approved by the designated state authority. Certified treatment programs shall dispense and use methadone in oral form only and according to the treatment requirements stipulated in the Federal Opioid Treatment Standards (42 CFR 8.12).¹⁻⁴

For induction/initial dosing for detoxification and maintenance treatment of opioid dependence, the total daily dose of methadone on the first day of treatment should not ordinarily exceed 40 mg. For the titration and maintenance treatment of opioid dependence, clinical stability is most commonly achieved at doses between 80 to 120 mg/day.¹⁻⁴

The methadone products targeted on this quantity limit criteria are indicated for opioid dependence only. These products should not be dispensed by a pharmacy when being used for opioid dependence.¹⁻⁶ However, in the event that these products are prescribed off-label for pain, the limits for methadone concentrate and dispersible tablets are set to accommodate a 3-day supply.

If the patient is requesting more than the initial quantity limit, then the claim will reject with a message indicating that quantity limits are exceeded.

REFERENCES

## LIMIT CRITERIA

These limits accumulate together across all drugs and strengths up to the highest quantity listed depending on the order that the claims are processed.

<table>
<thead>
<tr>
<th>Drug</th>
<th>1 Month Limit*</th>
<th>3 Month Limit*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methadose 10 mg/mL</td>
<td>30 mL/25 days**</td>
<td>30 mL/75 days**</td>
</tr>
<tr>
<td>(methadone oral concentrate)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methadose 40 mg</td>
<td>9 tablets/25 days**</td>
<td>9 tablets/75 days**</td>
</tr>
<tr>
<td>(methadone dispersible tablet)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.

** The 1 month, 3 month, retail, and mail limits will be the same.
SPECIALTY GUIDELINE MANAGEMENT

MIACALCIN (calcitonin [salmon] injection)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Miacalcin injection is indicated for the treatment of symptomatic Paget’s disease of bone in patients with moderate to severe disease characterized by polyostotic involvement with elevated serum alkaline phosphatase and urinary hydroxyproline excretion. There is no evidence that the prophylactic use of calcitonin salmon is beneficial in asymptomatic patients. Miacalcin injection should be used only in patients who do not respond to alternative treatments or for whom such treatments are not suitable.
   2. Miacalcin injection is indicated for the early treatment of hypercalcemic emergencies, along with other appropriate agents, when a rapid decrease in serum calcium is required, until more specific treatment of the underlying disease can be accomplished. It may also be added to existing therapeutic regimens for hypercalcemia such as intravenous fluids and furosemide, oral phosphate or corticosteroids, or other agents.
   3. Miacalcin injection is indicated for the treatment of postmenopausal osteoporosis in women greater than 5 years postmenopause. Fracture reduction efficacy has not been demonstrated. Miacalcin injection should be reserved for patients for whom alternative treatments are not suitable.

B. Compendial Uses
   Management of pain following an osteoporotic vertebral fracture

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Paget’s disease of bone: Supporting chart notes or medical record indicating a failed treatment or intolerance to an injectable bisphosphonate
B. Postmenopausal osteoporosis: Supporting chart notes or medical record indicating pretreatment T-score, as applicable to section III.
C. For management of pain following an osteoporotic vertebral fracture: Supporting chart notes or imaging report verifying osteoporotic spinal compression fracture

III. CRITERIA FOR INITIAL APPROVAL

A. Paget’s disease of bone
   Authorization of 12 months may be granted for treatment of Paget’s disease of bone when all of the following criteria are met:
1. Member has symptoms of Paget’s disease of bone (e.g., bone pain, bowing of lower extremity, hearing loss, heart failure, increased cardiac output, osteoarthritis) prior to therapy.
2. Member has failed prior treatment with an injectable bisphosphonate (e.g., pamidronate, zoledronic acid) or is intolerant to previous injectable therapy.

B. Hypercalcemia
Authorization of 1 month may be granted for treatment of hypercalcemic emergency when Miacalcin is used in combination with other agent(s) to reduce serum calcium levels.

C. Postmenopausal osteoporosis
Authorization of 12 months may be granted for postmenopausal osteoporosis when ALL of the following criteria are met:
1. Member is greater than 5 years postmenopause.
2. Member has a pre-treatment T-score less than or equal to -2.5.
3. Member has failed prior treatment with or is intolerant to previous injectable osteoporosis therapy (e.g., zoledronic acid [Reclast], teriparatide [Forteo], denosumab [Prolia]) OR has had an oral bisphosphonate trial of at least 1-year duration.

D. Management of pain following an osteoporotic vertebral fracture
Authorization of up to 28 days may be granted for treatment of pain following an osteoporotic vertebral fracture with osteoporosis when all of the following criteria are met:
1. Osteoporotic spinal compression fracture has been verified on imaging with correlating clinical signs and symptoms suggesting an acute injury. The date of imaging must be 0 to 5 days after an identifiable event or onset of symptoms and within 4 weeks of this request.
2. Member is neurologically intact.

IV. CONTINUATION OF THERAPY
A. Paget’s disease of bone
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for Paget’s disease of bone when member has experienced symptomatic improvement.

B. Postmenopausal osteoporosis
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for postmenopausal osteoporosis when member has experienced clinical benefit after at least 24 months of therapy with Miacalcin as evidenced by improvement or stabilization in T-score.

C. Other indications
All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

ZAVESCA (miglustat)
miglustat (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Zavesca is indicated as monotherapy for the treatment of adult patients with mild to moderate type 1 Gaucher disease for whom enzyme replacement therapy is not a therapeutic option (e.g. due to allergy, hypersensitivity, or poor venous access).

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Gaucher disease type 1
Authorization of 24 months may be granted for treatment of Gaucher disease type 1 when the diagnosis of Gaucher disease was confirmed by enzyme assay demonstrating a deficiency of beta-glucocerebrosidase (glucosidase) enzyme activity or by genetic testing.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

MIRCERA (methoxy polyethylene glycol-epoetin beta)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Mircera is indicated for the treatment of anemia associated with chronic kidney disease (CKD) in:

- Adult patients on dialysis and adult patients not on dialysis.
- Pediatric patients 5 to 17 years of age on hemodialysis who are converting from another erythropoiesis-stimulating agent (ESA) after their hemoglobin level was stabilized with an ESA.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Note: Requirements regarding hemoglobin level exclude values due to recent transfusion. All members must be assessed for iron deficiency anemia and have adequate iron stores or are receiving iron therapy before starting Mircera. Members may not use Mircera concomitantly with other erythropoiesis stimulating agents.

Anemia Due to Chronic Kidney Disease
Authorization of 12 weeks may be granted for the treatment of anemia due to chronic kidney disease when the pretreatment hemoglobin is less than 10 g/dL.

III. CONTINUATION OF THERAPY

Note: Requirements regarding current hemoglobin level exclude values due to recent transfusion. Members may not use Mircera concomitantly with other erythropoiesis stimulating agents.

Anemia Due to Chronic Kidney Disease
1. Authorization of 12 weeks may be granted for continuation of therapy when the current hemoglobin is < 12 g/dL and the member has shown a response to therapy with a rise in hemoglobin of ≥ 1 g/dL after at least 12 weeks of ESA therapy.
2. Authorization of up to 12 weeks may be granted for continuation of therapy in members who have not completed 12 weeks of ESA therapy.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

Mitoxantrone

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Acute nonlymphocytic leukemia (ANLL)
   Mitoxantrone in combination with other approved drug(s) is indicated in the initial therapy of ANLL in adults. This category includes myelogenous, promyelocytic, monocytic, and erythroid acute leukemias.

2. Multiple sclerosis
   Mitoxantrone is indicated for reducing neurologic disability and/or the frequency of clinical relapses in patients with secondary (chronic) progressive, progressive relapsing, or worsening relapsing-remitting multiple sclerosis (MS) (i.e., patients whose neurologic status is significantly abnormal between relapses). Mitoxantrone is not indicated in the treatment of patients with primary progressive MS.

3. Prostate cancer
   Mitoxantrone in combination with corticosteroids is indicated as initial chemotherapy for the treatment of patients with pain related to advanced hormone-refractory prostate cancer.

B. Compendial Uses

1. Acute lymphoblastic leukemia
2. Breast cancer
3. Hodgkin lymphoma
4. Liver carcinoma
5. Malignant lymphoma, indolent
6. Non-Hodgkin’s lymphoma with following subtypes
   a. AIDS-related B-cell lymphoma
   b. Diffuse large B-cell lymphoma
   c. Follicular lymphoma
   d. Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma
   e. Mantle cell lymphoma
   f. T-cell prolymphocytic leukemia
   g. Post-transplant proliferative disorders
7. Ovarian cancer

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Acute lymphoblastic leukemia (ALL)

Mitoxantrone 1662-A SGM P2019

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Authorization of 6 months may be granted for treatment of ALL.

B. **Acute nonlymphocytic leukemia (ANLL)¹⁻³,⁵**
   Authorization of 6 months may be granted for treatment of ANLL, including acute myeloid leukemia (AML) and acute promyelocytic leukemia (APL).

C. **Multiple sclerosis¹**
   Authorization of 1 dose (3 months) may be granted for treatment of multiple sclerosis.

D. **Prostate cancer¹⁻³,⁸**
   Authorization of 6 months may be granted for treatment of prostate cancer.

E. **Breast cancer²**
   Authorization of 6 months may be granted for treatment of breast cancer.

F. **Hodgkin lymphoma³,⁴**
   Authorization of 6 months may be granted for treatment of Hodgkin lymphoma.

G. **Liver carcinoma²**
   Authorization of 6 months may be granted for treatment of liver carcinoma.

H. **Non-Hodgkin's lymphoma (NHL)³,⁶,⁷**
   Authorization of 6 months may be granted for treatment of one of the following subtypes of NHL:
   1. AIDS-related B-cell lymphoma
   2. Diffuse large B-cell lymphoma
   3. Follicular lymphoma
   4. Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma
   5. Mantle cell lymphoma
   6. T-cell prolymphocytic leukemia
   7. Post-transplant proliferative disorders

I. **Ovarian cancer²**
   Authorization of 6 months may be granted for treatment of ovarian cancer.

J. **Malignant lymphoma, indolent²**
   Authorization of 6 months may be granted for treatment of malignant indolent lymphoma.

III. **CONTINUATION OF THERAPY**

A. **Multiple Sclerosis**
   Authorization of 3 months may be granted for continued treatment in members requesting reauthorization for multiple sclerosis (MS) who experienced a benefit from therapy (e.g., reduced neurologic disability, reduced frequency of clinical relapses).

B. **All Other Diagnoses (Excluding Multiple Sclerosis)**
   Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for all indications listed in Section II (excluding MS) who have not experienced an unacceptable toxicity.

IV. **REFERENCES**

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SPECIALTY GUIDELINE MANAGEMENT

MOZOBIL (plerixafor)

POLICY

I. INDICATIONS
The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Mozobil is indicated in combination with granulocyte-colony stimulating factor (G-CSF) to mobilize hematopoietic stem cells (HSCs) to the peripheral blood for collection and subsequent autologous transplantation in patients with non-Hodgkin’s lymphoma and multiple myeloma.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Hematopoietic Stem Cell Mobilization (HSCs) 1-6
Authorization of 6 months may be granted for the treatment of non-Hodgkin’s lymphoma (NHL) and multiple myeloma when ALL of the following criteria are met:
A. Mozobil will be used to mobilize hematopoietic stem cells for collection prior to autologous transplantation
B. Mozobil will be used in combination with G-CSF (e.g., filgrastim, pegfilgrastim)

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

MULPLETA (lusutrombopag)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Mulpleta is indicated for the treatment of thrombocytopenia in adult patients with chronic liver disease who are scheduled to undergo a procedure.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: pretreatment platelet count

III. CRITERIA FOR APPROVAL

Thrombocytopenia in chronic liver disease
Authorization of 30 days may be granted for treatment of thrombocytopenia in members with chronic liver disease when all of the following criteria are met:
A. Member has a baseline platelet count of less than 50 x 10⁹/L taken within 14 days of the request.
B. Member is scheduled to undergo a procedure.
C. Mulpleta will not be used in combination with other thrombopoietin receptor agonists (e.g., Doptelet, Promacta, Nplate) or with spleen tyrosine kinase inhibitors (e.g., Tavalisse).

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

MYALEPT (metreleptin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
   Myalept is indicated as an adjunct to diet as replacement therapy to treat the complications of leptin deficiency in patients with congenital or acquired generalized lipodystrophy.

   Limitations of Use:
   1. The safety and effectiveness of Myalept for the treatment of complications of partial lipodystrophy have not been established.
   2. The safety and effectiveness of Myalept for the treatment of liver disease, including nonalcoholic steatohepatitis (NASH), have not been established.
   3. Myalept is not indicated for use in patients with HIV-related lipodystrophy.
   4. Myalept is not indicated for use in patients with metabolic disease, including diabetes mellitus and hypertriglyceridemia, without concurrent evidence of congenital or acquired generalized lipodystrophy.

B. Compendial Use
   Partial lipodystrophy in patients with confirmed leptin deficiency and metabolic abnormalities

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: leptin level (for initial requests)

III. EXCLUSIONS

Coverage will not be provided for members with any of the following exclusions:
A. HIV-related lipodystrophy
B. Generalized obesity not associated with generalized lipodystrophy

IV. CRITERIA FOR INITIAL APPROVAL

Lipodystrophy
Authorization of 6 months may be granted for treatment of lipodystrophy when ALL of the following criteria are met:
A. Member has a diagnosis of congenital generalized lipodystrophy (i.e., Berardinelli-Seip syndrome), acquired generalized lipodystrophy (i.e., Lawrence syndrome), or partial lipodystrophy
B. Member has leptin deficiency confirmed by laboratory testing (i.e., less than 12ng/ml)\(^7\)\(^8\)
C. Member has at least one complication of lipodystrophy (e.g., diabetes mellitus, hypertriglyceridemia, increased fasting insulin level)

V. CONTINUATION OF THERAPY

Lipodystrophy
Authorization of 12 months may be granted to members requesting continuation of treatment for lipodystrophy when ALL of the following criteria are met:
A. All initial authorization criteria are met
B. Member has experienced an improvement from baseline in metabolic control (e.g., improved glycemic control, decrease in triglycerides, decrease in hepatic enzyme levels)

VI. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

Mylotarg (gemtuzumab ozogamicin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
1. Newly diagnosed CD33-positive acute myeloid leukemia in adults
2. Relapsed or refractory CD33-positive AML in adults and pediatric patients 2 years and older

Compendial Use
Mylotarg is indicated in high risk patients with acute promyelocytic leukemia (APL).

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Acute Myeloid Leukemia (AML)/ Acute Promyelocytic Leukemia (APL)
Authorization of 12 months may be granted for the treatment of AML/APL if the tumor is CD33-positive as confirmed by testing or analysis to identify the CD33 antigen.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

MYOBLOC (rimabotulinumtoxin B)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
A. Cervical dystonia in adults to reduce the severity of abnormal head position and neck pain associated with cervical dystonia
B. Treatment of chronic sialorrhea in adults

All other indications are considered experimental/investigational and are not a covered benefit.

II. EXCLUSIONS

Coverage will not be provided for cosmetic use.

III. CRITERIA FOR INITIAL APPROVAL

A. Cervical Dystonia
   Authorization of 24 months may be granted for treatment of cervical dystonia (e.g., torticollis).

B. Chronic sialorrhea
   Authorization of 24 months may be granted for treatment of chronic sialorrhea.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

NAGLAZYME (galsulfase)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Naglazyme is indicated for patients with Mucopolysaccharidosis VI (MPS VI, Maroteaux-Lamy syndrome). Naglazyme has been shown to improve walking and stair-climbing capacity.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Mucopolysaccharidosis VI (MPS VI)
Indefinite authorization may be granted for treatment of MPS VI when the diagnosis of MPS VI was confirmed by enzyme assay demonstrating a deficiency of N-acetylgalactosamine 4-sulfatase (arylsulfatase B) enzyme activity or by genetic testing.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

NATPARA (parathyroid hormone)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Natpara is indicated as an adjunct to calcium and vitamin D to control hypocalcemia in patients with hypoparathyroidism.

Limitations of Use:

- Because of the potential risk of osteosarcoma, Natpara is recommended only for patients who cannot be well-controlled on calcium supplements and active forms of vitamin D alone.
- Natpara was not studied in patients with hypoparathyroidism caused by calcium-sensing receptor mutations.
- Natpara was not studied in patients with acute post-surgical hypoparathyroidism.

All other indications are considered experimental/investigational and are not a covered benefit.

II. EXCLUSIONS

Coverage will not be provided for members with the following exclusion:

Acute postsurgical hypoparathyroidism (within 6 months of surgery) and expected recovery from the hypoparathyroidism

III. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review:

A. Lab results confirming serum parathyroid hormone concentrations below the lower limit of normal for the laboratory reference range on 2 separate days (at least 21 days apart) within the last 12 months
B. Lab results confirming magnesium levels within normal laboratory limits
C. Lab results confirming 25-hydroxyvitamin D concentration above the lower limit of normal laboratory range
D. Lab results confirming serum calcium is above 7.5mg/dL prior to initiating therapy with the requested medication

IV. CRITERIA FOR INITIAL APPROVAL
Authorization of 12 months may be granted for members who are initiating treatment with Natpara for the treatment of hypocalcemia associated with hypoparathyroidism who meet all of the following:
A. Member has hypocalcemia and concomitant serum parathyroid hormone concentrations below the lower limit of normal for the laboratory reference range on at least 2 separate dates at least 21 days apart within the last 12 months
B. Member is receiving vitamin D metabolite/analog therapy with calcitriol greater than or equal to 0.25 mcg per day or alphacalcidol greater than or equal to 0.5 mcg/day (or equivalent)
C. Member is receiving supplemental calcium treatment greater than or equal to 1000 mg/day over and above normal dietary calcium intake
D. Serum magnesium levels within normal laboratory limits
E. Serum 25-hydroxyvitamin D concentration above the lower limit of normal laboratory range
F. Serum calcium is greater than 7.5mg/dL prior to initiating therapy with the requested medication

V. CONTINUATION OF THERAPY

Authorization of 12 months will be granted for continued treatment in members requesting reauthorization for an indication listed in Section IV who are experiencing benefit from therapy as evidenced by having an increase in calcium and parathyroid hormone level from baseline.

VI. REFERENCES

PRIOR AUTHORIZATION CRITERIA

BRAND NAME* (generic)

NAYZILAM (midazolam nasal spray)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization
Ref # 3102-C

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS
Nayzilam is indicated for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient’s usual seizure pattern in patients with epilepsy 12 years of age and older.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from the patient’s usual seizure pattern in a patient with epilepsy
- The patient is 12 years of age or older

Quantity Limits apply.

RATIONALE
Nayzilam is indicated for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient’s usual seizure pattern in patients with epilepsy 12 years of age and older. Patients and caregivers should be instructed on what is and is not an intermittent and stereotypic episode of increased seizure activity (i.e., seizure cluster) that is appropriate for treatment, and the timing of administration in relation to the onset of the episode. The initial dose of Nayzilam is one spray (5 mg dose) administered into one nostril. If needed, one additional spray (5 mg dose) may be administered into the opposite nostril after 10 minutes if the patient has not responded to the initial dose. A second dose of Nayzilam should not be administered if the patient has trouble breathing or if there is excessive sedation that is uncharacteristic of the patient during a seizure cluster episode. Do not use more than 2 doses of Nayzilam to treat a single episode. It is recommended that Nayzilam be used to treat no more than 1 episode every three days and no more than 5 episodes per month.

Nayzilam is supplied as a solution of midazolam. Each single-dose nasal spray unit delivers 5 mg of midazolam in 0.1 mL of solution. Nayzilam is supplied in boxes of 2 nasal spray units, each contained within an individual blister pack. Because it is not recommended to treat more than 5 episodes per month and each episode could require up to 2 doses, the limit will be set at 5 boxes, 10 nasal spray units.

REFERENCES
CRITERIA FOR APPROVAL

1. Is the requested drug being prescribed for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from the patient’s usual seizure pattern in a patient with epilepsy?
   - Yes
   - No

2. Is the patient 12 years of age or older?
   - Yes
   - No

3. Does the patient require more than the plan allowance of 10 nasal spray units per month?
   - Yes
   - No
   [RPh Note: If yes, then deny and enter a partial approval for 10 nasal spray units per month of Nayzilam.]

Mapping Instructions

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Go to 2</td>
</tr>
<tr>
<td></td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you meet all of the following: - You have epilepsy - The requested drug is being used for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from your usual seizure pattern</td>
</tr>
<tr>
<td></td>
<td>Your request has been denied based on the information we have.</td>
</tr>
<tr>
<td></td>
<td>[Short Description: No approvable diagnosis]</td>
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<tr>
<td>2.</td>
<td>Go to 3</td>
</tr>
<tr>
<td></td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you are 12 years of age or older.</td>
</tr>
<tr>
<td></td>
<td>Your request has been denied based on the information we have.</td>
</tr>
<tr>
<td></td>
<td>[Short Description: No approvable diagnosis]</td>
</tr>
<tr>
<td>3.</td>
<td>Deny</td>
</tr>
<tr>
<td></td>
<td>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 10 nasal spray units/month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.</td>
</tr>
<tr>
<td></td>
<td>[Short Description: Over max quantity]</td>
</tr>
</tbody>
</table>
SPECIALTY GUIDELINE MANAGEMENT

NERLYNX (neratinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Nerlynx is indicated for the extended adjuvant treatment of adult patients with early stage human epidermal growth factor receptor (HER)2-overexpressed/amplified breast cancer, to follow adjuvant trastuzumab based therapy.

B. Compendial Uses
Metastatic central nervous system (CNS) lesions if active against primary tumor (breast)

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Breast cancer
Authorization of up to 12 months total may be granted for the treatment of early stage HER2-positive breast cancer when Nerlynx is initiated after completing adjuvant trastuzumab based therapy.

B. Metastatic CNS lesions
Authorization of 12 months may be granted for the treatment of metastatic CNS lesions from HER2-positive breast cancer.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

NEULASTA (pegfilgrastim)
FULPHILA (pegfilgrastim-jmdp)
UDENYCA (pegfilgrastim-cbqv)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Neulasta
1. Patients with Cancer Receiving Myelosuppressive Chemotherapy
   Neulasta is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.
2. Hematopoietic Syndrome of Acute Radiation Syndrome
   Neulasta is indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome).

Fulphila
Patients with Cancer Receiving Myelosuppressive Chemotherapy
Fulphila is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

Udenyca
Patients with Cancer Receiving Myelosuppressive Chemotherapy
Udenyca is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

B. Compendial Use

1. Stem cell transplantation-related indications
2. Prophylaxis for chemotherapy-induced febrile neutropenia in patients with solid tumors
3. Radiation therapy/injury
4. Hairy cell leukemia
5. Chronic Myeloid Leukemia (CML)

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

A. Primary Prophylaxis of Febrile Neutropenia
1. Documentation must be provided of the member’s diagnosis and chemotherapeutic regimen.
2. If chemotherapeutic regimen has an intermediate risk of febrile neutropenia (10-19% [See Appendix B]), documentation must be provided outlining the patient’s risk factors that confirm the member is at high risk for febrile neutropenia.

III. CRITERIA FOR INITIAL APPROVAL

A. Prevention of neutropenia in cancer patients receiving myelosuppressive chemotherapy

Authorization of 6 months may be granted for prevention of febrile neutropenia when all of the following criteria are met (1, 2, 3, and 4):

1. The requested medication will not be used in combination with other colony stimulating factors within any chemotherapy cycle.
2. The member will not be receiving concurrent chemotherapy and radiation therapy.
3. The requested medication will not be administered with weekly chemotherapy regimens.
4. One of the following criteria is met (i or ii):
   i. The requested medication will be used for primary prophylaxis in members with a solid tumor or non-myeloid malignancies who have received, are currently receiving, or will be receiving myelosuppressive anti-cancer therapy that is expected to result in 20% or higher incidence of FN (See Appendix A) OR 10 – 19% risk of FN (See Appendix B) and who are considered to be at high risk of FN because of bone marrow compromise or co-morbidity, including any of the following (not an all-inclusive list):
      a. Active infections, open wounds, or recent surgery
      b. Age greater than or equal to 65 years
      c. Bone marrow involvement by tumor producing cytopenias
      d. Previous chemotherapy or radiation therapy
      e. Poor nutritional status
      f. Poor performance status
      g. Previous episodes of FN
      h. Other serious co-morbidities, including renal dysfunction, liver dysfunction, HIV infection, cardiovascular disease
      i. Persistent neutropenia
   ii. The requested medication will be used for secondary prophylaxis in members with solid tumors or non-myeloid malignancies who experienced a febrile neutropenic complication or a dose-limiting neutropenic event (a nadir or day of treatment count impacting the planned dose of chemotherapy) from a prior cycle of similar chemotherapy, with the same dose and scheduled planned for the current cycle (for which primary prophylaxis was not received).

B. Other indications

Authorization of 6 months may be granted for members with any of the following indications:

1. Stem cell transplantation-related indications
2. Radiation therapy/injury
   i. Manage neutropenia in members acutely exposed to myelosuppressive doses of radiation therapy
   ii. Treatment of radiation injury
3. Hairy cell leukemia
   Individuals with hairy cell leukemia with neutropenic fever following chemotherapy.
4. Chronic Myeloid Leukemia
   Individuals with Chronic Myeloid Leukemia (CML) for treatment of resistant neutropenia due to tyrosine kinase inhibitor therapy

IV. CONTINUATION OF THERAPY
All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. APPENDIX
A. APPENDIX A: Selected Chemotherapy Regimens with an Incidence of Febrile Neutropenia of 20% or Higher

1. Acute Lymphoblastic Leukemia:
   Select ALL regimens as directed by treatment protocol (see NCCN guidelines)

2. Bladder Cancer:
   i. Dose dense MVAC (methotrexate, vinblastine, doxorubicin, cisplatin)
   ii. CBDCa/Pac (carboplatin, paclitaxel)

3. Bone Cancer:
   i. VAI (vincristine, doxorubicin or dactinomycin, ifosfamide)
   ii. VDC-IE (vincristine, doxorubicin or dactinomycin, and cyclophosphamide alternating with ifosfamide and etoposide)
   iii. VIDE (vincristine, ifosfamide, doxorubicin or dactinomycin, etoposide)

4. Breast Cancer:
   i. Docetaxel + trastuzumab
   ii. Dose-dense AC followed by T (doxorubicin, cyclophosphamide, paclitaxel)
   iii. TAC (docetaxel, doxorubicin, cyclophosphamide)
   iv. AT (doxorubicin, docetaxel)
   v. Doc (docetaxel)
   vi. TC (docetaxel, cyclophosphamide)
   vii. TCH (docetaxel, carboplatin, trastuzumab)

5. Esophageal and Gastric Cancers:
   Docetaxel/cisplatin/fluorouracil (5-FU)

6. Head and Neck Squamous Cell Carcinoma:
   TPF (docetaxel, cisplatin, fluorouracil [5-FU])

7. Hodgkin Lymphoma:
   i. Brentuximab vedotin + AVD (doxorubicin, vinblastine, dacarbazine)
   ii. Escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)

8. Kidney Cancer:
   Doxorubicin/gemcitabine

9. Non-Hodgkin’s Lymphoma:
   i. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)
   ii. ICE (ifosfamide, carboplatin, etoposide)
   iii. Dose-dense CHOP-14 (cyclophosphamide, doxorubicin, vincristine, prednisone) + rituximab
   iv. MINE (mesna, ifosfamide, novantrone, etoposide)
   v. DHAP (dexamethasone, cisplatin, cytarabine)
   vi. ESHAP (etoposide, methylprednisolone, cisplatin, cytarabine (Ara-C))
   vii. HyperCVAD + rituximab (cyclophosphamide, vincristine, doxorubicin, dexamethasone + rituximab)
   viii. VAPEC-B (vincristine, doxorubicin, prednisolone, etoposide, cyclophosphamide, bleomycin)

10. Melanoma:
    Dacarbazine-based combination with IL-2, interferon alpha (dacarbazine, cisplatin, vinblastine, IL-2, interferon alpha)

11. Multiple Myeloma:
    i. DT-PACE (dexamethasone/thalidomide/cisplatin/ doxorubicin/cyclophosphamide/etoposide) + bortezomib (VTD-PACE)
ii. DT-PACE (dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide)

12. Ovarian Cancer:
   i. Topotecan
   ii. Docetaxel

13. Soft Tissue Sarcoma:
   i. MAID (mesna, doxorubicin, ifosfamide, dacarbazine)
   ii. Doxorubicin
   iii. Ifosfamide/doxorubicin

14. Small Cell Lung Cancer:
   i. Top (topotecan)
   ii. CAV (cyclophosphamide, doxorubicin, vincristine)

15. Testicular Cancer:
   i. VelP (vinblastine, ifosfamide, cisplatin)
   ii. VIP (etoposide, ifosfamide, cisplatin)
   iii. TIP (paclitaxel, ifosfamide, cisplatin)

B. APPENDIX B: Selected Chemotherapy Regimens with an Incidence of Febrile Neutropenia of 10% to 19%

1. Occult Primary – Adenocarcinoma:
   Gemcitabine/docetaxel

2. Bone Cancer:
   i. Cisplatin/doxorubicin
   ii. VDC (cyclophosphamide, vincristine, doxorubicin or dactinomycin)

3. Breast Cancer:
   i. Docetaxel
   ii. CMF classic (cyclophosphamide, methotrexate, fluorouracil [5-FU])
   iii. CA (doxorubicin, cyclophosphamide) (60 mg/m2) (hospitalized)
   iv. AC (doxorubicin, cyclophosphamide) + sequential docetaxel (taxane portion only)
   v. AC + sequential docetaxel + trastuzumab
   vi. A (doxorubicin) (75 mg/m2)
   vii. AC (doxorubicin, cyclophosphamide)
   viii. CapDoc (capecitabine, docetaxel)
   ix. Paclitaxel every 21 days

4. Cervical Cancer:
   i. Irinotecan
   ii. Cisplatin/topotecan
   iii. Paclitaxel/cisplatin
   iv. Topotecan

5. Colorectal Cancer:
   i. FL (fluorouracil [5-FU], leucovorin)
   ii. CPT-11 (irinotecan) (350 mg/m2 q 3 wk)
   iii. FOLFOX (fluorouracil [5-FU], leucovorin, oxaliplatin)

6. Esophageal and Gastric Cancers:
   i. Irinotecan/cisplatin
   ii. Epirubicin/cisplatin/fluorouracil (5-FU)
   iii. Epirubicin/cisplatin/capecitabine

7. Head and Neck Cancers:
   Cis/Doc/5-FU (cisplatin, docetaxel, fluorouracil [5-FU])

8. Non-Hodgkin’s Lymphoma:
   i. EPOCH-IT chemotherapy
   ii. GDP (gemcitabine, dexamethasone, cisplatin/carboplatin)
iii. GDP (gemcitabine, dexamethasone, cisplatin/carboplatin) + rituximab
iv. FMR (fludarabine, mitoxantrone, rituximab)
v. CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) including regimens with pegylated liposomal doxorubicin
vi. CHOP + rituximab (cyclophosphamide, doxorubicin, vincristine, prednisone, rituximab) including regimens with pegylated liposomal doxorubicin

9. Non-Small Cell Lung Cancer:
i. Cisplatin/paclitaxel
ii. Cisplatin/vinorelbine
iii. Cisplatin/docetaxel
iv. Cisplatin/etoposide
v. Carboplatin/paclitaxel
vi. Docetaxel

10. Ovarian Cancer:
Carboplatin/docetaxel

11. Pancreatic Cancer:
FOLFiRINOX (folinic acid [leucovorin], fluorouracil [5-FU], irinotecan and oxaliplatin)

12. Prostate Cancer:
Cabazitaxel

13. Small Cell Lung Cancer:
Etoposide/carboplatin

14. Testicular Cancer:
i. BEP (bleomycin, etoposide, cisplatin)
ii. Etoposide/cisplatin

15. Uterine Sarcoma:
Docetaxel

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

NEUPOGEN (filgrastim)
GRANIX (tbo-filgrastim)
ZARXIO (filgrastim-sndz)
NIVESTYM (filgrastim-aafi)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Neupogen

1. Patients with Cancer Receiving Myelosuppressive Chemotherapy
   Neupogen is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever.

2. Patients With Acute Myeloid Leukemia Receiving Induction or Consolidation Chemotherapy
   Neupogen is indicated for reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of adults with acute myeloid leukemia.

3. Patients with Cancer Receiving Bone Marrow Transplant
   Neupogen is indicated to reduce the duration of neutropenia and neutropenia-related clinical sequelae, (e.g., febrile neutropenia) in patients with non-myeloid malignancies undergoing myeloablative chemotherapy followed by marrow transplantation.

4. Patients Undergoing Autologous Peripheral Blood Progenitor Cell Collection and Therapy
   Neupogen is indicated for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.

5. Patients With Severe Chronic Neutropenia
   Neupogen is indicated for chronic administration to reduce the incidence and duration of sequelae of neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.

Nivestym

1. Patients with Cancer Receiving Myelosuppressive Chemotherapy
   Nivestym is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever.

2. Patients With Acute Myeloid Leukemia Receiving Induction or Consolidation Chemotherapy
Nivestym is indicated for reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of adults with acute myeloid leukemia.

3. Patients with Cancer Receiving Bone Marrow Transplant
   Nivestym is indicated to reduce the duration of neutropenia and neutropenia-related clinical sequelae, (e.g., febrile neutropenia) in patients with non-myeloid malignancies undergoing myeloablative chemotherapy followed by marrow transplantation.

4. Patients Undergoing Autologous Peripheral Blood Progenitor Cell Collection and Therapy
   Nivestym is indicated for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.

5. Patients With Severe Chronic Neutropenia
   Nivestym is indicated for chronic administration to reduce the incidence and duration of sequelae of neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.

Granix
Granix is indicated to reduce the duration of severe neutropenia in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

Zarxio
1. Patients with Cancer Receiving Myelosuppressive Chemotherapy
   a. Zarxio is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever.

2. Patients With Acute Myeloid Leukemia Receiving Induction or Consolidation Chemotherapy
   a. Zarxio is indicated for reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of adults with acute myeloid leukemia.

3. Patients with Cancer Undergoing Bone Marrow Transplant
   a. Zarxio is indicated to reduce the duration of neutropenia and neutropenia-related clinical sequelae, (e.g., febrile neutropenia) in patients with non-myeloid malignancies undergoing myeloablative chemotherapy followed by marrow transplantation.

4. Patients Undergoing Autologous Peripheral Blood Progenitor Cell Collection and Therapy
   a. Zarxio is indicated for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.

5. Patients With Severe Chronic Neutropenia
   a. Zarxio is indicated for chronic administration to reduce the incidence and duration of sequelae of neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.

B. Compendial Uses (Neupogen/Granix/Zarxio/Nivestym)
   1. Treatment of chemotherapy-induced febrile neutropenia in patients with non-myeloid malignancies
   2. Treatment of anemia in patients with myelodysplastic syndromes (MDS)
   3. Treatment of neutropenia in patients with MDS
   4. Following chemotherapy for acute lymphocytic leukemia (ALL)
   5. Stem cell transplantation-related indications
   6. Agranulocytosis
   7. Aplastic anemia
   8. Neutropenia related to HIV/AIDS
9. Neutropenia related to renal transplantation

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Neutropenia in cancer patients receiving myelosuppressive chemotherapy

Authorization of 6 months may be granted for prevention or treatment of febrile neutropenia when both of the following criteria are met:

1. Member has a non-myeloid malignancy and has received, is currently receiving, or will be receiving myelosuppressive anti-cancer therapy
2. The requested drug will not be administered less than 24 hours before or after chemotherapy or radiotherapy

B. Other indications

Authorization of 6 months may be granted for members with any of the following indications:

1. Agranulocytosis
2. Aplastic anemia
3. Neutropenia related to HIV/AIDS
4. Neutropenia related to renal transplantation
5. Acute myeloid leukemia
6. Stem cell transplantation-related indications
7. Severe chronic neutropenia (congenital, cyclic, or idiopathic)
8. Myelodysplastic syndrome (anemia or neutropenia)

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

MEDICAL NECESSITY CRITERIA

MEDICAL NECESSITY CRITERIA (NEW TO MARKET DRUGS)

Status: CVS Caremark Criteria
Type: Medical Necessity Criteria
Ref # 1175-A

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:
• The requested drug is being used for an FDA-Approved indication OR an indication supported in the compendia of current literature (examples: AHFS, Micromedex, current accepted guidelines)
AND
• The prescribed quantity falls within the manufacturer’s published dosing guidelines or within dosing guidelines found in the compendia of current literature (examples: package insert, AHFS, Micromedex, current accepted guidelines)
AND
• The patient had an inadequate treatment response or intolerance to all formulary alternatives for the given diagnosis (or to at least 1 agent within each of a given class of agents when more than 1 class is available for the diagnosis) OR
• The patient has a contraindication to all formulary alternatives OR
• This is the only FDA-Approved product for the patient’s diagnosis.

RATIONALE
The intent of the criteria is to ensure that patients follow selection elements noted in labeling and/or practice guidelines in order to decrease the potential for inappropriate utilization. The intent of this Formulary Exception program is to confirm the appropriate coverage of a non-formulary prescription medication for patients. These criteria apply to all medications subject to formulary exception not otherwise managed through drug specific Prior Authorization criteria.

This policy is intended to ensure that medications subject to formulary exception under the CVS Health National Formulary are utilized in accordance with FDA indications and uses found in the compendia of current literature including American Hospital Formulary Service Drug Information (AHFS), Micromedex, or current accepted guidelines. This policy also aims to insure that non-formulary medications are approved within manufacturer’s dosing guidelines or dosing guidelines of current compendia and to foster cost-effective, first-line use of available formulary/preferred drug list medications.

In addition, if the patient has tried and had an inadequate treatment response, intolerance, or contraindication to all formulary alternatives (generics and/or formulary brands), OR, there are no other FDA-Approved products for the patient’s diagnosis, the prior authorization will be approved.

REFERENCES
N/A

Written by: UM Development (PL)
Date Written: 08/2014
Revised: (NB) 10/2014, 02/2015, 02/2016, (TM) 03/2016 (add Q1&2), (TM/JK) 06/2016 (add Q3, and e.g.), (NB) 09/2016 (moved #5, separated #6 & #7, rewored #8), (TM) 12/2016 (#3 e.g.), (changed duration to 12 mos), (TM, NB) 02/2017 (remove questions 1,2,3, changed reqd # to all)), (TM) 02/2018 (no clinical changes), (TM) 02/2019 (no clinical changes)
Reviewed: Medical Affairs (LCB) 08/2014, 10/2014, (SS) 02/2015, 02/2016, (WF) 03/2016, (WF) 06/2016, (AN) 02/2017

New To Market Drugs Medical Necessity 1175-A 02-2019 ©2019 CVS Caremark. All rights reserved.

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**CRITERIA FOR APPROVAL**

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<th>Question</th>
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<tr>
<td>1</td>
<td>Is the requested drug being used for an FDA-Approved indication or an indication supported in the compendia of current literature (examples: AHFS, Micromedex, current accepted guidelines)?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>Does the prescribed quantity fall within the manufacturer’s published dosing guidelines or within dosing guidelines found in the compendia of current literature (examples: package insert, AHFS, Micromedex, current accepted guidelines)?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>Has the patient had an inadequate treatment response or intolerance to all formulary alternatives for the given diagnosis (or to at least 1 agent within each of a given class of agents when more than 1 class is available for the diagnosis)? [If yes, then no further questions.]</td>
<td>Yes</td>
<td>No</td>
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<tr>
<td>4</td>
<td>Does the patient have a contraindication to all formulary alternatives? [If yes, then no further questions.]</td>
<td>Yes</td>
<td>No</td>
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<td>5</td>
<td>Is this the only FDA-Approved product to treat the patient’s diagnosis?</td>
<td>Yes</td>
<td>No</td>
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**Mapping Instructions**

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<tr>
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<td>Approve, 12 months</td>
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SPECIALTY GUIDELINE MANAGEMENT

NEXAVAR (sorafenib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Hepatocellular carcinoma
      Nexavar is indicated for the treatment of patients with unresectable hepatocellular carcinoma (HCC).
   2. Renal cell carcinoma
      Nexavar is indicated for the treatment of patients with advanced renal cell carcinoma (RCC).
   3. Differentiated thyroid carcinoma
      Nexavar is indicated for the treatment of locally recurrent or metastatic, progressive, differentiated thyroid carcinoma (DTC) that is refractory to radioactive iodine treatment.

B. Compendial Uses
   1. Hepatocellular carcinoma (Child-Pugh Class A or B7)
      a. Patients who have unresectable disease and are not a transplant candidate
      b. Patients who are inoperable by performance status or comorbidity, or have local disease or local disease with minimal extrahepatic disease only
      c. Patients who have metastatic disease or extensive liver tumor burden
      d. Subsequent treatment as a single-agent for patients who have progressed after first-line lenvatinib
   2. Acute myeloid leukemia
      a. In combination with azacitidine or decitabine in patients age ≥ 60 years with FLT3-ITD mutation as low-intensity treatment induction when not a candidate for intensive induction therapy or declines intensive therapy
      b. In combination with azacitidine or decitabine in patients age ≥ 60 years with FLT3-ITD mutation, as post-remission therapy following response to previous lower intensity therapy with the same regimen
      c. A component of repeating the initial successful induction if late relapse (greater than or equal to 12 months) for relapsed or refractory disease
      d. In combination with azacitidine or decitabine for relapsed or refractory disease
   3. Soft tissue sarcoma subtypes
      a. Angiosarcoma, as single agent therapy
      b. Desmoid tumors (aggressive fibromatosis), primary, recurrent, or progressive disease
      c. Solitary fibrous tumor, as single-agent therapy
      d. Hemangiopericytoma, as single-agent therapy
      e. Leiomyosarcoma
   4. Gastrointestinal stromal tumors (GIST), treatment for disease progression after single-agent therapy with imatinib, sunitinib and regorafenib
   5. Thyroid carcinoma (medullary carcinoma, papillary carcinoma, Hürthle cell carcinoma, or follicular)
   6. Relapsed/refractory bone cancer, as second-line therapy as a single agent for the following subtypes:
      a. Osteosarcoma
b. Dedifferentiated chondrosarcoma
c. High-grade undifferentiated pleomorphic sarcoma (UPS)
7. Recurrent chordoma
8. Epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer; if platinum-resistant, in combination with topotecan for persistent disease or recurrence

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION
Submission of the following information is necessary to initiate the prior authorization review: FLT3-ITD mutation testing results (where applicable)

III. CRITERIA FOR INITIAL APPROVAL

A. Hepatocellular Carcinoma
1. Authorization of 12 months may be granted for treatment of unresectable or metastatic hepatocellular carcinoma.
2. Authorization of 12 months may be granted for treatment of hepatocellular carcinoma for subsequent treatment as a single agent for members who progressed after first-line lenvatinib.

B. Acute Myeloid Leukemia
Authorization of 12 months may be granted for treatment of acute myeloid leukemia when either of the following criteria are met:
1. Nexavar will be used in combination with azacitidine or decitabine in members age 60 or older with FLT3-ITD mutation as low-intensity treatment induction or post-remission therapy; OR
2. Nexavar will be used for relapsed/refractory disease as either:
   a. A component of repeating the initial successful induction if late relapse (greater than or equal to 12 months); OR
   b. In combination with azacitidine or decitabine if the member is FLT3-ITD mutation positive.

C. Soft Tissue Sarcoma
1. Authorization of 12 months may be granted for treatment of leiomyosarcoma.
2. Authorization of 12 months may be granted for treatment of angiosarcoma, solitary fibrous tumor, or hemangiopericytoma as single agent therapy.
3. Authorization of 12 months may be granted for treatment of primary, recurrent, or progressive desmoid tumor/aggressive fibromatosis.

D. Gastrointestinal Stromal Tumor (GIST)
Authorization of 12 months may be granted for treatment of gastrointestinal stromal tumor for disease progression after single-agent therapy with imatinib, sunitinib, and regorafenib.

E. Renal Cell Carcinoma
Authorization of 12 months may be granted for treatment of advanced renal cell carcinoma.

F. Differentiated Thyroid Carcinoma
Authorization of 12 months may be granted for treatment of progressive and/or symptomatic radioiodine refractory papillary, Hürthle cell, or follicular thyroid carcinoma.

G. Medullary Thyroid Carcinoma
Authorization of 12 months may be granted for treatment of medullary thyroid carcinoma when either of the following criteria are met:
1. Member has an intolerance or contraindication to vandetanib (Caprelsa) AND cabozantinib (Cometriq), OR
2. Member has disease progression while on vandetanib (Caprelsa) or cabozantinib (Cometriq).

H. Bone Cancer
1. Authorization of 12 months may be granted for treatment as second-line therapy for relapsed/refractory or metastatic disease as a single agent for the following types of bone cancer:
   a. Osteosarcoma
   b. Dedifferentiated chondrosarcoma
   c. High-grade undifferentiated pleomorphic sarcoma (UPS)

I. Chordoma
Authorization of 12 months may be granted for treatment of recurrent chordoma as a single agent.

J. Epithelial Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer
Authorization of 12 months may be granted for treatment of epithelial ovarian, fallopian tube, or primary peritoneal cancer if the disease is platinum-resistant and Nexavar is given in combination with topotecan for persistent disease or recurrence.

IV. CONTINUATION OF THERAPY
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication in Section III who are clinically benefiting from therapy or who have not experienced an unacceptable toxicity.

V. REFERENCES
Specialty Guideline Management

NINLARO (ixazomib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Ninlaro is indicated in combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received at least one prior therapy.

B. Compendial Uses

Multiple myeloma

1. In combination with lenalidomide and dexamethasone as primary therapy for active (symptomatic) myeloma or disease relapse after 6 months following primary induction therapy with the same regimen
2. In combination with dexamethasone for patients who have received at least one prior therapy for previously treated myeloma for relapsed or progressive disease
3. In combination with dexamethasone and pomalidomide for patients who have received at least two prior therapies including an immunomodulatory agent and a proteasome inhibitor and who have demonstrated disease progression on or within 60 days of completion of the last therapy for previously treated myeloma for relapsed or progressive disease

All other indications are considered experimental/investigational and are not covered benefits.

II. CRITERIA FOR INITIAL APPROVAL

Multiple Myeloma

Authorization of 12 months may be granted for treatment of multiple myeloma when any of the following criteria is met:

1. Ninlaro is prescribed in combination with lenalidomide and dexamethasone, or
2. Ninlaro is prescribed in combination with dexamethasone for patients with relapsed or progressive disease, or
3. Ninlaro is prescribed in combination with dexamethasone and pomalidomide for patients who have received at least two prior therapies.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

NORTHERA (droxidopa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Treatment of orthostatic dizziness, lightheadedness, or the “feeling that you are about to black out” in adult patients with symptomatic neurogenic orthostatic hypotension (NOH) caused by primary autonomic failure [Parkinson's disease (PD), multiple system atrophy, and pure autonomic failure], dopamine beta-hydroxylase deficiency, and non-diabetic autonomic neuropathy. Effectiveness beyond 2 weeks of treatment has not been established. The continued effectiveness of Northera should be assessed periodically.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Neurogenic orthostatic hypotension
Authorization of 3 months may be granted for treatment of neurogenic orthostatic hypotension when all of the following criteria are met:
A. Member has a persistent, consistent decrease in SBP of at least 20 mmHg or decrease in DBP of at least 10 mmHg within 3 minutes of standing.
B. Member has neurogenic orthostatic hypotension due to ONE of the following diagnoses:
   1. Primary autonomic failure due to Parkinson’s disease, multiple system atrophy, and pure autonomic failure, OR
   2. Dopamine beta hydroxylase deficiency, OR
   3. Non-diabetic autonomic neuropathy

III. CONTINUATION OF THERAPY

Neurogenic orthostatic hypotension
Authorization of 3 months may be granted for treatment of neurogenic orthostatic hypotension when all of the following criteria are met:
A. Member has experienced a sustained decrease in dizziness
B. Member has neurogenic orthostatic hypotension due to ONE of the following diagnoses:
   1. Primary autonomic failure due to Parkinson’s disease, multiple system atrophy, and pure autonomic failure, OR
   2. Dopamine beta hydroxylase deficiency, OR
   3. Non-diabetic autonomic neuropathy
IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

NOVOSEVEN RT (coagulation factor VIIa [recombinant])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Hemophilia A or hemophilia B with inhibitors
   2. Congenital factor VII deficiency
   3. Glanzmann’s thrombasthenia
   4. Acquired hemophilia

B. Compendial Uses
   1. Acquired von Willebrand syndrome
   2. Inhibitors to factor XI

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Congenital Factor VII Deficiency
   Indefinite authorization may be granted for treatment of congenital factor VII deficiency.

B. Hemophilia A with Inhibitors
   Indefinite authorization may be granted for treatment of hemophilia A with inhibitors (see Appendix) when the inhibitor titer is ≥ 5 Bethesda units per milliliter (BU/mL) or the member has a history of an inhibitor titer ≥ 5 BU.

C. Hemophilia B with Inhibitors
   Indefinite authorization may be granted for treatment of hemophilia B with inhibitors (see Appendix) when the inhibitor titer is ≥ 5 Bethesda units per milliliter (BU/mL) or the member has a history of an inhibitor titer ≥ 5 BU.

D. Glanzmann’s Thrombasthenia
   Indefinite authorization may be granted to members for treatment of Glanzmann’s thrombasthenia.

E. Acquired Hemophilia
   Indefinite authorization may be granted for treatment of acquired hemophilia.
F. Acquired von Willebrand Syndrome
Indefinite authorization may be granted for treatment of acquired von Willebrand syndrome when other therapies failed to control the member’s condition (e.g., desmopressin or factor VIII/von Willebrand factor).

G. Inhibitors to Factor XI
Indefinite authorization may be granted for treatment of members with inhibitors to factor XI.

III. CONTINUATION OF THERAPY
All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. APPENDIX

Appendix: Inhibitors - Bethesda Units (BU)
The presence of inhibitors is confirmed by a specific blood test called the Bethesda inhibitor assay.

- High-titer inhibitors:
  - > 5 BU/mL
  - Inhibitors act strongly and quickly neutralize factor

- Low-titer inhibitors:
  - < 5 BU/mL
  - Inhibitors act weakly and slowly neutralize factor

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

NPLATE (romiplostim)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Treatment of thrombocytopenia in patients with chronic immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Chronic or persistent primary immune thrombocytopenia (ITP)
Authorization of 6 months may be granted to members with chronic or persistent ITP who meet all of the following criteria:

A. Inadequate response or intolerance to prior therapy with corticosteroids, immunoglobulins, or splenectomy
B. Untransfused platelet count at time of diagnosis is less than 30x10^9/L OR 30x10^9/L to 50x10^9/L with symptomatic bleeding (e.g., significant mucous membrane bleeding, gastrointestinal bleeding or trauma) or risk factors for bleeding (see Section IV).

III. CONTINUATION OF THERAPY

Chronic or persistent ITP
A. Authorization of 12 months may be granted to members with current platelet count less than or equal to 200x10^9/L.
B. Authorization of 12 months may be granted to members with current platelet count greater than 200 x10^9/L for whom Nplate dosing will be adjusted to achieve a platelet count sufficient to avoid clinically important bleeding.

IV. APPENDIX

Examples of risk factors for bleeding (not all inclusive)

- Undergoing a medical or dental procedure where blood loss is anticipated
- Comorbidity (e.g., peptic ulcer disease, hypertension)
- Mandated anticoagulation therapy
• Profession (e.g., construction worker) or lifestyle (e.g., plays contact sports) that predisposes patient to trauma

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

NUBEQA (darolutamide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication [1]
Nubeqa is indicated for the treatment of patients with non-metastatic castration-resistant prostate cancer.

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided if the requested medication is used in combination with a second-generation oral anti-androgen (e.g., apalutamide [Erleada]) or an oral androgen metabolism inhibitor (e.g., abiraterone acetate [Zytiga]).

III. CRITERIA FOR INITIAL APPROVAL

Prostate Cancer [1]
Authorization of 12 months may be granted to members for the treatment of non-metastatic castration-resistant prostate cancer when the member has had a bilateral orchiectomy or will be using the requested medication in combination with a GnRH analog.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III if who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

NUCALA (mepolizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
1. Maintenance Treatment of Severe Asthma
   Nucala is an interleukin-5 antagonist monoclonal antibody (IgG1 kappa) indicated for add-on maintenance treatment of patients with severe asthma aged 12 years and older, and with an eosinophilic phenotype.

   Limitations of Use: Not for relief of acute bronchospasm or status asthmaticus

2. Eosinophilic Granulomatosis with Polyangiitis
   Nucala is indicated for the treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA).

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Asthma
   Authorization of 12 months may be granted for treatment of asthma when all of the following criteria are met:
   1. Member is 12 years of age or older.
   2. Member has a baseline blood eosinophil count of at least 150 cells per microliter.
   3. Member has inadequate asthma control (e.g., hospitalization or emergency medical care visit within the past year) despite current treatment with both of the following medications at optimized doses:
      a. Inhaled corticosteroid
      b. Additional controller (long acting beta2-agonist, leukotriene modifier, or sustained-release theophylline)

B. Eosinophilic Granulomatosis with Polyangiitis
   Authorization of 12 months may be granted for treatment of eosinophilic granulomatosis with polyangiitis when all of the following criteria are met:
   1. Member is 18 years of age or older.
   2. Member has a history or the presence of an eosinophil count of more than 1000 cells per microliter or a blood eosinophil level of greater than 10%.
III. CONTINUATION OF THERAPY

A. Asthma
   Authorization of 12 months may be granted for continuation of treatment of asthma when all of the following criteria are met:
   1. Member is 12 years of age or older.
   2. Asthma control has improved on Nucala treatment as demonstrated by at least one of the following:
      a. A reduction in the frequency and/or severity of symptoms and exacerbations
      b. A reduction in the daily maintenance oral corticosteroid dose

B. Eosinophilic Granulomatosis with Polyangiitis
   Authorization of 12 months may be granted for continuation of treatment of eosinophilic granulomatosis with polyangiitis when all of the following criteria are met:
   1. Member is 18 years of age or older.
   2. Member has beneficial response to treatment with Nucala as demonstrated by any of the following:
      a. A reduction in the frequency of relapses, or
      b. A reduction in the daily oral corticosteroid dose, or
      c. No active vasculitis

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

NUCALA (mepolizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
A. Nucala is indicated for add-on maintenance treatment of patients with severe asthma aged 12 years and older, and with an eosinophilic phenotype.
B. Nucala is indicated for the treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA).

Limitations of Use: Not for relief of acute bronchospasm or status asthmaticus

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review (initial requests only):
A. Asthma: Member’s chart or medical record showing baseline blood eosinophil count
B. EGPA: Member’s chart or medical record showing blood eosinophil count or level as noted in section III.B.2. below

III. CRITERIA FOR INITIAL APPROVAL

A. Asthma
Authorization of 6 months may be granted for treatment of asthma when all of the following criteria are met:
1. Member is 12 years of age or older.
2. Member has a baseline blood eosinophil count of at least 150 cells per microliter.
3. Member has inadequate asthma control (e.g., hospitalization or emergency medical care visit within the past year) despite current treatment with both of the following medications at optimized doses:
   a. Inhaled corticosteroid
   b. Additional controller (long acting beta2-agonist, leukotriene modifier, or sustained-release theophylline)
4. Member will not use Nucala as monotherapy.
5. Member does not currently smoke.
6. Member will not use Nucala concomitantly with other biologics (e.g., Cinqair, Dupixent, Fasenra, Xolair).
B. Eosinophilic granulomatosis with polyangiitis
Authorization of 12 months may be granted for treatment of eosinophilic granulomatosis with polyangiitis when all of the following criteria are met:
1. Member is 18 years of age or older.
2. Member has a history or the presence of an eosinophil count of more than 1000 cells per microliter or a blood eosinophil level of greater than 10%.
3. Member has at least two of the following disease characteristics of EGPA:
   a. Biopsy showing histopathological evidence of eosinophilic vasculitis, perivascular eosinophilic infiltration, or eosinophil-rich granulomatous inflammation
   b. Neuropathy, mono or poly (motor deficit or nerve conduction abnormality)
   c. Pulmonary infiltrates, non-fixed; sino-nasal abnormality
   d. Cardiomyopathy (established by echocardiography or magnetic resonance imaging)
   e. Glomerulonephritis (hematuria, red cell casts, proteinuria)
   f. Alveolar hemorrhage (by bronchoalveolar lavage)
   g. Palpable purpura
   h. Anti-neutrophil cytoplasmic anti-body (ANCA) positive (Myeloperoxidase or proteinase 3)
4. Member has had at least one relapse (requiring increase in oral corticosteroids dose, initiation/increased dose of immunosuppressive therapy or hospitalization) within 2 years prior to starting treatment with Nucala or has a refractory disease.

IV. CONTINUATION OF THERAPY

A. Asthma
Authorization of 12 months may be granted for continuation of treatment of asthma when all of the following criteria are met:
1. Member is 12 years of age or older.
2. Asthma control has improved on Nucala treatment as demonstrated by at least one of the following:
   a. A reduction in the frequency and/or severity of symptoms and exacerbations
   b. A reduction in the daily maintenance oral corticosteroid dose
3. Member will not use Nucala as monotherapy.
4. Member does not currently smoke.
5. Member will not use Nucala concomitantly with other biologics (e.g., Cinqair, Dupixent, Fasenra, Xolair).

B. Eosinophilic granulomatosis with polyangiitis
Authorization of 12 months may be granted for continuation of treatment of eosinophilic granulomatosis with polyangiitis when all of the following criteria are met:
1. Member is 18 years of age or older.
2. Member has beneficial response to treatment with Nucala as demonstrated by any of the following:
   a. A reduction in the frequency of relapses, or
   b. A reduction in the daily oral corticosteroid dose, or
   c. No active vasculitis

V. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

NUPLAZID (pimavanserin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Nuplazid is indicated for the treatment of hallucinations and delusions associated with Parkinson’s disease psychosis.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for initial treatment of hallucinations and delusions associated with Parkinson’s disease psychosis when the member has mild or no cognitive impairment as determined by physician’s clinical diagnosis and/or cognitive impairment screening tests (e.g. Mini-Mental Status Examination [MMSE], Montreal Cognitive Assessment [MOCA])

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment of hallucinations and delusions associated with Parkinson’s disease psychosis when the member has experienced improvement in psychotic symptoms (hallucinations and/or delusions) since starting therapy

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

OBIZUR (antihemophilic factor [recombinant], porcine sequence)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Obizur is indicated for the treatment of bleeding episodes in adults with acquired hemophilia A.

Limitations of Use:
A. Safety and efficacy of Obizur has not been established in patients with a baseline anti-porcine factor VIII inhibitor titer of greater than 20 BU.
B. Obizur is not indicated for the treatment of congenital hemophilia A or von Willebrand disease.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Acquired hemophilia A
Authorization of 1 month may be granted for treatment of acquired hemophilia A.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

OCALIVA (obeticholic acid)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Ocaliva is indicated for the treatment of primary biliary cholangitis (PBC) in combination with ursodeoxycholic acid (UDCA) in adults with an inadequate response to UDCA, or as monotherapy in adults unable to tolerate UDCA. This indication is approved under accelerated approval based on a reduction in alkaline phosphatase (ALP). An improvement in survival or disease-related symptoms has not been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. For initial requests: Pretreatment serum alkaline phosphatase (ALP) level
B. For continuation of therapy: Current serum alkaline phosphatase (ALP) and/or current total bilirubin level

III. CRITERIA FOR INITIAL APPROVAL

Primary biliary cholangitis (PBC) (previously known as primary biliary cirrhosis)

Authorization of 6 months may be granted for treatment of PBC in members 18 years of age or older when all of the following criteria are met:

A. Diagnosis of PBC is confirmed by at least two of the following three criteria:
   1. Biochemical evidence of cholestasis with elevation of alkaline phosphatase (ALP) level for at least 6 months duration
   2. Presence of antimitochondrial antibodies (AMA) (titer >1:40 by immunofluorescence or immunoenzymatic reactivity) or PBC-specific antinuclear antibodies (ANA) (eg, anti-gp210, anti-sp100)
   3. Histologic evidence of PBC on liver biopsy (eg, non-suppurative inflammation and destruction of interlobular and septal bile ducts)
B. Member has an elevated serum ALP level prior to initiation of therapy with obeticholic acid
C. Member meets at least one of the following requirements:
   1. Inadequate response to at least 12 months of prior therapy with ursodeoxycholic acid (UDCA)/ursodiol and the member will continue concomitant therapy with UDCA/ursodiol, or
   2. Intolerance to UDCA/ursodiol

IV. CONTINUATION OF THERAPY
Authorization of 12 months may be granted for members who have achieved or maintained a clinical benefit from Ocaliva therapy (i.e., at least a 15% reduction in ALP level, ALP level less than 1.67-times ULN, or total bilirubin less than or equal to ULN).

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

OCREVUS (ocrelizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications:
Ocrevus is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. Ocrevus is also indicated for the treatment of primary progressive MS, in adults.

All other indications are considered experimental/investigational and are not covered benefits.

II. CRITERIA FOR INITIAL APPROVAL

A. Relapsing Forms of Multiple Sclerosis
Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

B. Clinically isolated syndrome
Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome of multiple sclerosis.

C. Primary Progressive Multiple Sclerosis
Authorization of 12 months may be granted to members for the treatment of primary progressive MS.

III. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted for members who are experiencing disease stability or improvement while receiving Ocrevus.

IV. OTHER CRITERIA

Members will not use Ocrevus concomitantly with other medications used for the treatment of multiple sclerosis, excluding Ampyra.

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

SANDOSTATIN (octreotide acetate injection)
SANDOSTATIN LAR DEPOT (octreotide acetate for injectable suspension)
octreotide acetate injection

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. octreotide acetate/Sandostatin:
      a. Indicated to reduce blood levels of growth hormone and IGF-1 (somatomedin C) in acromegaly patients who have had inadequate response to or cannot be treated with surgical resection, pituitary irradiation, and bromocriptine mesylate at maximally tolerated doses.
      b. Indicated for the symptomatic treatment of patients with metastatic carcinoid tumors where it suppresses or inhibits the severe diarrhea and flushing episodes associated with the disease.
      c. Indicated for the treatment of the profuse watery diarrhea associated with vasoactive intestinal peptide (VIP)-secreting tumors.

   2. Sandostatin LAR: Sandostatin LAR Depot is indicated in patients in whom initial treatment with Sandostatin injection has been shown to be effective and tolerated.
      a. Indicated for long-term maintenance therapy in acromegalic patients who have had an inadequate response to surgery and/or radiotherapy, or for whom surgery and/or radiotherapy is not an option.
      b. Indicated for long-term treatment of the severe diarrhea and flushing episodes associated with metastatic carcinoid tumors.
      c. Indicated for long-term treatment of the profuse watery diarrhea associated with vasoactive intestinal peptide (VIP)-secreting tumors.

B. Compendial Uses
   1. Neuroendocrine tumors (NETs):
      a. Tumors of the gastrointestinal (GI) tract, lung, and thymus (carcinoid tumors)
      b. Tumors of the pancreas
   2. Meningiomas
   3. Thymomas and thymic carcinomas
   4. Congenital hyperinsulinism (CHI)/persistent hyperinsulinemic hypoglycemia of infancy (PHHI) (octreotide and Sandostatin only)

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Acromegaly
   Authorization of 24 months may be granted for the treatment of acromegaly when all of the following criteria are met:
1. Member has a high pretreatment insulin-like growth factor-1 (IGF-1) level for age and/or gender based on the laboratory reference range.
2. Member had an inadequate or partial response to surgery or radiotherapy OR there is a clinical reason why the member has not had surgery or radiotherapy.

B. Neuroendocrine tumors (NETs)
   1. Tumors of the gastrointestinal (GI) tract (carcinoid tumor)
      Authorization of 24 months may be granted for treatment of NETs of the GI tract.
   2. Tumors of the thymus (carcinoid tumor)
      Authorization of 24 months may be granted for treatment of NETs of the thymus.
   3. Tumors of the lung (carcinoid tumor)
      Authorization of 24 months may be granted for treatment of NETs of the lung.
   4. Tumors of the pancreas
      Authorization of 24 months may be granted for treatment of NETs of the pancreas.

C. Carcinoid syndrome
   Authorization of 24 months may be granted for treatment of carcinoid syndrome.

D. Vasoactive intestinal peptide tumors (VIPomas)
   Authorization of 24 months may be granted for management of symptoms related to hormone hypersecretion of VIPomas.

E. Meningiomas
   Authorization of 24 months may be granted to members for treatment of unresectable meningioma.

F. Thymomas and thymic carcinomas
   Authorization of 24 months may be granted for treatment of thymomas and thymic carcinomas.

G. Congenital hyperinsulinism (CHI)/persistent hyperinsulinemic hypoglycemia of infancy (octreotide and Sandostatin only)
   Authorization of 6 months may be granted for treatment of CHI and persistent hyperinsulinemic hypoglycemia in an infant.

III. CONTINUATION OF THERAPY

A. Acromegaly
   Authorization of 24 months may be granted for continuation of therapy for acromegaly when the member’s IGF-1 level has decreased or normalized since initiation of therapy.

B. All other indications
   Members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

ODOMZO (sonidegib)

POLICY

I. INDICATIONS
The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Odomzo is indicated for the treatment of adult patients with locally advanced basal cell carcinoma (BCC) that has recurred following surgery or radiation therapy, or those who are not candidates for surgery or radiation therapy.

Compendial Uses
Nodal or distant metastatic basal cell carcinoma

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Basal Cell Carcinoma
Authorization of 12 months may be granted for treatment of locally advanced or metastatic basal cell carcinoma.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in Section II when there is no evidence of unacceptable toxicity or disease progression on the current regimen.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

OFEV (nintedanib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Ofev is indicated for the treatment of idiopathic pulmonary fibrosis.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Idiopathic Pulmonary Fibrosis (IPF)
Authorization of 24 months may be granted for treatment of idiopathic pulmonary fibrosis when the member has undergone a diagnostic work-up which includes the following:

1. Other known causes of interstitial lung disease (e.g., domestic and occupational environmental exposures, connective tissue disease, drug toxicity) have been excluded AND
2. The member has completed a high-resolution computed tomography (HRCT) study of the chest or a lung biopsy which reveals a result consistent with the usual interstitial pneumonia (UIP) pattern, OR has completed an HRCT study of the chest which reveals a result other than the UIP pattern (e.g., probable UIP, indeterminate for UIP) and the diagnosis is supported by a lung biopsy. If a lung biopsy has not been previously conducted, the diagnosis is supported by a multidisciplinary discussion between a radiologist and pulmonologist who are experienced in IPF.

III. CONTINUATION OF THERAPY

Idiopathic Pulmonary Fibrosis (IPF)
All members (including new members) requesting authorization for continuation of therapy may be granted an authorization of 24 months when the member is currently receiving treatment with Ofev, excluding when Ofev is obtained as samples or via manufacturer’s patient assistance programs.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

OLUMIANT (baricitinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Olumiant is indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more TNF antagonist therapies.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Moderately to severely active rheumatoid arthritis (RA)
A. Authorization of 24 months may be granted for treatment of moderately to severely active RA for members who have previously received treatment with Olumiant.

B. Authorization of 24 months may be granted for treatment of moderately to severely active RA for members who have experienced an inadequate response or intolerance to at least one tumor necrosis factor (TNF) inhibitor.

III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Olumiant as evidenced by low disease activity or improvement in signs and symptoms of RA.

IV. OTHER

Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB).

Note: Members who have received Olumiant or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) are exempt from requirements related to TB screening in this Policy.

V. REFERENCES

1. Olumiant [package insert]. Indianapolis, IN: Lilly USA, LLC; May 2018.
SPECIALTY GUIDELINE MANAGEMENT

OLYSIO (simeprevir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Olysio is indicated for the treatment of adults with chronic hepatitis C virus (HCV) infection:

A. in combination with sofosbuvir in patients with HCV genotype 1 without cirrhosis or with compensated cirrhosis
B. in combination with peginterferon alfa (PEG-IFN) and ribavirin (RBV) in patients with HCV genotype 1 or 4 without cirrhosis or with compensated cirrhosis

All other indications are considered experimental/investigational and are not a covered benefit.

II. EXCLUSIONS

Coverage will not be provided for members with decompensated cirrhosis/moderate or severe hepatic impairment (Child Turcotte Pugh Class B or C).

Note: When the requested drug is being used in a combination therapy regimen, exclusions to the other antiviral drugs also apply.

III. INITIAL CRITERIA FOR APPROVAL

A. Chronic hepatitis C virus infection, in combination with PEG-IFN and RBV

1. Genotype 1 or 4 infection

   Authorization of up to 6 weeks total may be granted for initiation of therapy in members who are treatment-naïve or failed prior treatment with PEG-IFN and RBV AND meet one of the following criteria:
   a. Genotype 1a infection without the NS3 Q80K polymorphism
   b. Genotype 1b infection
   c. Genotype 4 infection

B. Chronic hepatitis C virus infection, in combination with Sovaldi

1. Genotype 1a infection

   a. Authorization of up to 12 weeks total may be granted for members without cirrhosis who are treatment-naïve or failed prior treatment with PEG-IFN and RBV.
   b. Authorization of up to 24 weeks total may be granted for members with compensated cirrhosis without the NS3 Q80K polymorphism who are treatment-naïve or failed prior treatment with PEG-IFN and RBV.

2. Genotype 1b infection
a. Authorization of up to 12 weeks total may be granted for members without cirrhosis who are treatment-naïve or failed prior treatment with PEG-IFN and RBV.
b. Authorization of up to 24 weeks total may be granted for members with compensated cirrhosis who are treatment-naïve or failed prior treatment with PEG-IFN and RBV.

3. Recurrent HCV infection post liver transplantation
   Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have recurrent HCV genotype 1 or 4 infection post liver transplantation.

C. Chronic hepatitis C virus infection, in combination with Sovaldi and RBV
   Recurrent HCV infection post liver transplantation
   Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have recurrent HCV genotype 1 or 4 infection post liver transplantation.

D. HCV and HIV Coinfection
   Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A, B or C above are met.

IV. CONTINUATION OF THERAPY

Chronic hepatitis C virus infection, in combination with PEG-IFN and RBV
   Genotype 1 or 4 infection at week 4 assessment
   Authorization of up to 12 weeks total for Olysio and up to 48 weeks total for PEG-IFN and RBV may be granted for members with HCV-RNA < 25 IU/mL at week 4 of treatment.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

ONCASPAR (pegaspargase)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   Acute lymphoblastic leukemia (ALL):
   1. Oncaspar is indicated as a component of a multi-agent chemotherapeutic regimen for the first line treatment of patients with ALL.
   2. Oncaspar is indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of patients with ALL and hypersensitivity to native forms of L-asparaginase.

B. Compendial Uses
   1. Extranodal natural killer/T-cell lymphoma, nasal type: as a component of multi-agent chemotherapeutic regimen
   2. Lymphoblastic lymphoma (managed in the same manner as ALL)
   3. Induction/consolidation/relapsed/refractory therapy for Philadelphia chromosome-negative ALL as a component of multi-agent chemotherapeutic regimen
   4. Philadelphia chromosome-positive ALL as a component of a multi-agent chemotherapeutic regimen

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

1. Acute Lymphoblastic Leukemia (ALL) and Lymphoblastic Lymphoma
   Authorization of 12 months may be granted for the treatment of ALL or lymphoblastic lymphoma when Oncaspar is used in conjunction with multi-agent chemotherapy.

2. Extranodal Natural Killer/T-cell Lymphoma, nasal type
   Authorization of 12 months may be granted for the treatment of extranodal natural killer/T-cell lymphoma, nasal type when Oncaspar is used in conjunction with multi-agent chemotherapy.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

ONPATTRO (patisiran)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Onpattro is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Testing or analysis confirming a mutation of the TTR gene
B. Medical record documentation confirming the member demonstrates signs and symptoms of polyneuropathy and an improvement in these signs and symptoms since starting therapy for continuation

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a neurologist, geneticist, or physician specializing in the treatment of amyloidosis.

IV. CRITERIA FOR INITIAL APPROVAL

Polyneuropathy of Hereditary Transthyretin-mediated Amyloidosis
Authorization of 12 months may be granted for treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis (also called transthyretin-type familial amyloid polyneuropathy [ATTR-FAP]) when all of the following criteria are met:
A. The diagnosis is confirmed by detection of a mutation of the TTR gene.
B. Member exhibits clinical manifestations of ATTR-FAP (e.g., amyloid deposition in biopsy specimens, TTR protein variants in serum, progressive peripheral sensory-motor polyneuropathy).
C. The member is not a liver transplant recipient.
D. The requested medication will not be used in combination with inotersen (Tegsedi) or tafamidis.

V. CONTINUATION OF THERAPY
Authorization of 12 months may be granted for the continued treatment of ATTR-FAP when all of the following criteria are met:
A. The member must have met all initial authorization criteria.
B. The member must have demonstrated a beneficial response to treatment with Onpattro therapy compared to baseline (e.g., improvement of neuropathy severity and rate of disease progression as demonstrated by the modified Neuropathy Impairment Scale+7 (mNIS+7) composite score, the Norfolk Quality of Life-Diabetic Neuropathy (QoL-DN) total score, polyneuropathy disability (PND) score, FAP disease stage, manual grip strength). Documentation from the medical record must be provided.

REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

OPDIVO (nivolumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Unresectable or metastatic melanoma
   i. As a single agent for the treatment of patients with BRAF V600 wild-type unresectable or metastatic melanoma.
   ii. As a single agent for the treatment of patients with BRAF V600 mutation-positive unresectable or metastatic melanoma.
   iii. In combination with ipilimumab for the treatment of patients with unresectable or metastatic melanoma.

2. Adjuvant treatment of melanoma
   Opdivo is indicated for the adjuvant treatment of melanoma with lymph node involvement or metastatic disease who have undergone complete resection.

3. Metastatic non-small cell lung cancer (NSCLC)
   Opdivo is indicated for the treatment of patients with metastatic NSCLC with progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Opdivo.

4. Renal cell carcinoma (RCC)
   i. Opdivo is indicated for the treatment of patients with advanced RCC who have received prior anti-angiogenic therapy.
   ii. Opdivo is indicated for the treatment of patients with intermediate or poor risk, previously untreated advanced renal cell carcinoma, in combination with ipilimumab.

5. Classical Hodgkin lymphoma (cHL)
   Opdivo is indicated for the treatment of patients with cHL that has relapsed or progressed after:
   i. Autologous hematopoietic stem cell transplantation (HSCT) and brentuximab vedotin
   ii. 3 or more lines of therapy that includes autologous HSCT

6. Squamous Cell Carcinoma of the Head and Neck
   Opdivo is indicated for the treatment of patients with recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN) with disease progression on or after platinum-based therapy.

7. Urothelial Carcinoma (Bladder cancer, Upper Genitourinary tract tumors, Urothelial carcinoma of the prostate, Primary carcinoma of the urethra)
   Opdivo is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who:
   i. Have disease progression during or following platinum-containing chemotherapy
ii. Have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

8. Colorectal Cancer
Opdivo is indicated for adult and pediatric (12 years and older) patients with microsatellite instability-high or mismatch repair deficient metastatic colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan, as a single agent or in combination with ipilimumab.

9. Hepatocellular Carcinoma
Opdivo is indicated for the treatment of hepatocellular carcinoma who have been previously treated with sorafenib.

10. Small cell lung cancer
Opdivo is indicated for the treatment of patients with metastatic small cell lung cancer with progression after platinum-based chemotherapy and at least one other line of therapy.

B. Compendial Uses
1. Classical Hodgkin lymphoma
2. Colorectal cancer
3. Renal cell carcinoma (Kidney cancer)
4. Non-small cell lung cancer (NSCLC)
5. Small cell lung cancer
6. Uveal Melanoma
7. Anal Carcinoma
8. Merkel Cell Carcinoma
9. Central Nervous System (CNS) brain metastases in patients with melanoma
10. Hepatocellular Carcinoma (HCC) in patients previously treated with lenvatinib.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Unresectable or metastatic melanoma
Authorization of 12 months may be granted for the treatment of unresectable or metastatic melanoma.

B. Adjuvant treatment of melanoma
Authorization of 12 months may be granted for the adjuvant treatment of melanoma with lymph node involvement or metastatic disease who have undergone complete resection

C. Non-small cell lung cancer (NSCLC)
Authorization of 12 months may be granted for treatment of metastatic NSCLC when Opdivo is requested for disease progression on or after a first-line cytotoxic regimen or for further progression on other systemic therapy.

D. Renal cell carcinoma (Kidney cancer)
Authorization of 12 months may be granted for treatment of advanced, relapsed or unresectable renal cell carcinoma.

E. Classical Hodgkin lymphoma (cHL)
Authorization of 12 months may be granted for treatment of cHL.
F. Squamous cell carcinoma of the head and neck (SCCHN)  
Authorization of 12 months may be granted for treatment of recurrent or metastatic SCCHN in members with disease progression on or after platinum-based therapy.

G. Urothelial carcinoma (Bladder cancer, Upper Genitourinary tract tumors, Urothelial carcinoma of the prostate, Primary carcinoma of the urethra)  
Authorization of 12 months may be granted for treatment of locally advanced or metastatic urothelial carcinoma, including bladder cancer, upper genitourinary tract tumors, urothelial carcinoma of the prostate, or primary carcinoma of the urethra, when the member has experienced disease progression following platinum-containing chemotherapy.

H. Colorectal cancer  
Authorization of 12 months may be granted for treatment of unresectable, locally advanced, or metastatic colorectal cancer with deficient mismatch repair or high microsatellite instability.

I. Small cell lung cancer  
Authorization of 12 months may be granted for treatment of small cell lung cancer.

J. Hepatocellular carcinoma  
Authorization of 12 months may be granted for treatment of hepatocellular carcinoma for members who have been previously treated with sorafenib or lenvatinib.

K. Uveal Melanoma  
Authorization of 12 months may be granted for treatment of uveal melanoma.

L. Anal Carcinoma  
Authorization of 12 months may be granted for treatment of anal cancer.

M. Merkel Cell Carcinoma  
Authorization of 12 months may be granted for treatment of Merkel cell carcinoma.

N. CNS Brain Metastases  
Authorization of 12 months may be granted for treatment of CNS brain metastases in patients with melanoma.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

## STEP THERAPY WITH QUANTITY LIMIT AND POST LIMIT PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>EXTENDED-RELEASE OPIOID ANALGESICS</th>
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</thead>
<tbody>
<tr>
<td>BRAND NAME* <em>(generic)</em></td>
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</tr>
<tr>
<td>ARYMO ER</td>
<td>(morphine sulfate extended-release tablets)</td>
</tr>
<tr>
<td>AVINZA</td>
<td>(morphine extended-release capsules)</td>
</tr>
<tr>
<td>BELBUCA</td>
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</tr>
<tr>
<td>BUTRANS</td>
<td>(buprenorphine transdermal system)</td>
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<tr>
<td>CONZIP</td>
<td>(tramadol hydrochloride extended-release)</td>
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<tr>
<td>DOLOPHINE 5 MG, 10 MG</td>
<td>(methadone hydrochloride tablets)</td>
</tr>
<tr>
<td>DURAGESIC</td>
<td>(fentanyl transdermal system)</td>
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<td>(methadone hydrochloride tablets)</td>
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<td>XTAMPZA ER</td>
<td>(oxycodone extended-release capsules)</td>
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<td>ZOHYDRO ER</td>
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(hydrocodone bitartrate extended-release capsules)

**Status: CVS Caremark Criteria**

**Type: Initial Step Therapy; Initial Limit; Post Limit PA**

*Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

**FDA-APPROVED INDICATIONS**

**Arymo ER, Avinza, Kadian, MorphaBond ER, MS Contin, and Embeda**

Arymo ER, Avinza, Kadian, MorphaBond ER, MS Contin, and Embeda are indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

**Limitations of Use**

- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, reserve Arymo ER, Avinza, Kadian, MorphaBond ER, MS Contin, and Embeda for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.

- Arymo ER, Avinza, Kadian, MorphaBond ER, MS Contin, and Embeda are not indicated as an as-needed (prn) analgesic.

**Belbuca and Butrans**

Belbuca and Butrans are indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

**Limitations of Use**

- Because of the risks of addiction, abuse and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with long-acting opioid formulations, reserve Belbuca and Butrans for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.

- Belbuca and Butrans are not indicated as an as-needed (prn) analgesic.

**ConZip, Ultram ER, and Tramadol Hydrochloride Extended-Release**

ConZip, Ultram ER, and Tramadol Hydrochloride Extended-Release are indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

**Limitations of Use**

- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release/long-acting opioid formulations, reserve ConZip, Ultram ER, and Tramadol Hydrochloride Extended-Release for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.

- ConZip, Ultram ER, and Tramadol Hydrochloride Extended-Release is not indicated as an as-needed (prn) analgesic.

**Dolophine Tablets**

Dolophine tablets are indicated for the:

- Management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

**Limitations of Use**

- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with long-acting opioids, reserve Dolophine tablets for use in patients for whom alternative analgesic treatment options (e.g., non-opioid analgesics or immediate-release opioid
analgesics) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.

- Dolophine tablets are not indicated as an as-needed (prn) analgesic.
- Detoxification treatment of opioid addiction (heroin or other morphine-like drugs).
- Maintenance treatment of opioid addiction (heroin or other morphine-like drugs), in conjunction with appropriate social and medical services.

Limitations of Use
- Methadone products used for the treatment of opioid addiction in detoxification or maintenance programs are subject to the conditions for distribution and use required under 42 CFR 8.12.

**Duragesic**
Duragesic is indicated for the management of pain in opioid-tolerant patients, severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

Patients considered opioid-tolerant are those who are taking, for one week or longer, at least 60 mg morphine per day, 25 mcg transdermal fentanyl per hour, 30 mg oral oxycodone per day, 8 mg oral hydromorphone per day, 25 mg oral oxymorphone per day, 60 mg hydrocodone per day, or an equianalgesic dose of another opioid.

Limitations of Use
- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, reserve Duragesic for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.
- Duragesic is not indicated as an as-needed (prn) analgesic.

**Exalgo**
Exalgo is indicated for the management of pain in opioid-tolerant patients severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

Patients considered opioid tolerant are those who are receiving, for one week or longer, at least 60 mg oral morphine per day, 25 mcg transdermal fentanyl per hour, 30 mg oral oxycodone per day, 8 mg oral hydromorphone per day, 25 mg oral oxymorphone per day, 60 mg oral hydrocodone per day, or an equianalgesic dose of another opioid.

Limitations of Use
- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, reserve Exalgo for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.
- Exalgo is not indicated as an as-needed (prn) analgesic.

**Hysingla ER**
Hysingla ER is indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

Limitations of Use
- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, reserve Hysingla ER for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.
- Hysingla ER is not indicated as an as-needed (prn) analgesic.

**Methadone Injection**
Methadone Injection is indicated:
- For the management of pain severe enough to require an opioid analgesic and for which alternative treatment options are inadequate.

Limitations of Use
- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses reserve Methadone Hydrochloride Injection for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or opioid combination products):
  - Have not been tolerated, or are not expected to be tolerated,
  - Have not provided adequate analgesia, or are not expected to provide adequate analgesia.
• For use in temporary treatment of opioid dependence in patients unable to take oral medication.

Limitations of Use

- Injectable methadone products are not approved for the outpatient treatment of opioid dependence. In this patient population, parenteral methadone is to be used only for patients unable to take oral medication, such as hospitalized patients.

Conditions For Distribution And Use Of Methadone Products For The Treatment Of Opioid Addiction

Code of Federal Regulations, Title 42, Sec 8

Methadone products when used for the treatment of opioid addiction in detoxification or maintenance programs, shall be dispensed only by opioid treatment programs (and agencies, practitioners or institutions by formal agreement with the program sponsor) certified by the Substance Abuse and Mental Health Services Administration and approved by the designated state authority. Certified treatment programs shall dispense and use methadone in oral form only and according to the treatment requirements stipulated in the Federal Opioid Treatment Standards (42 CFR 8.12). See below for important regulatory exceptions to the general requirement for certification to provide opioid agonist treatment. Failure to abide by the requirements in these regulations may result in criminal prosecution, seizure of the drug supply, revocation of the program approval, and injunction precluding operation of the program.

Regulatory Exceptions To The General Requirement For Certification To Provide Opioid Agonist Treatment:

During inpatient care, when the patient was admitted for any condition other than concurrent opioid addiction [pursuant to 21CFR 1306.07(c)], to facilitate the treatment of the primary admitting diagnosis.

During an emergency period of no longer than 3 days while definitive care for the addiction is being sought in an appropriately licensed facility [pursuant to 21CFR 1306.07(b)].

Methadone Intensol

Methadone Hydrochloride Intensol (oral concentrate) is indicated for the:

• Management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

Limitations of Use

- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with long-acting opioids, reserve methadone for use in patients for whom alternative analgesic treatment options (e.g., non-opioid analgesics or immediate-release opioid analgesics) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.

- Methadone is not indicated as an as-needed (prn) analgesic.

• Detoxification treatment of opioid addiction (heroin or other morphine-like drugs).

• Maintenance treatment of opioid addiction (heroin or other morphine-like drugs), in conjunction with appropriate social and medical services.

Conditions For Distribution And Use Of Methadone Products For The Treatment Of Opioid Addiction

Code of Federal Regulations, Title 42, Sec 8

Methadone products when used for the treatment of opioid addiction in detoxification or maintenance programs, shall be dispensed only by opioid treatment programs (and agencies, practitioners or institutions by formal agreement with the program sponsor) certified by the Substance Abuse and Mental Health Services Administration and approved by the designated state authority. Certified treatment programs shall dispense and use methadone in oral form only and according to the treatment requirements stipulated in the Federal Opioid Treatment Standards (42 CFR 8.12). See below for important regulatory exceptions to the general requirement for certification to provide opioid agonist treatment. Failure to abide by the requirements in these regulations may result in criminal prosecution, seizure of the drug supply, revocation of the program approval, and injunction precluding operation of the program.

Regulatory Exceptions To The General Requirement For Certification To Provide Opioid Agonist Treatment:

During inpatient care, when the patient was admitted for any condition other than concurrent opioid addiction [pursuant to 21CFR 1306.07(c)], to facilitate the treatment of the primary admitting diagnosis.

During an emergency period of no longer than 3 days while definitive care for the addiction is being sought in an appropriately licensed facility [pursuant to 21CFR 1306.07(b)].

Methadone Oral Solution

Methadone Hydrochloride Oral Solution is indicated for the:

• Management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.
Limitations of Use

- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with long-acting opioids, reserve Methadone Hydrochloride Oral Solution for use in patients for whom alternative analgesic treatment options (e.g., non-opioid analgesics or immediate-release opioid analgesics) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.
- Methadone Hydrochloride Oral Solution is not indicated as an as-needed (prn) analgesic.
- Detoxification treatment of opioid addiction (heroin or other morphine-like drugs).
- Maintenance treatment of opioid addiction (heroin or other morphine-like drugs), in conjunction with appropriate social and medical services.

Limitations of Use

- Methadone products used for the treatment of opioid addiction in detoxification or maintenance programs are subject to the conditions for distribution and use required under 42 CFR 8.2.

Methadone Tablets

Methadone Hydrochloride tablets are indicated for the:

- Management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

Limitations of Use

- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with long-acting opioids, reserve Methadone Hydrochloride Tablets for use in patients for whom alternative analgesic treatment options (e.g., non-opioid analgesics or immediate-release opioid analgesics) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.
- Methadone Hydrochloride Tablets are not indicated as an as-needed (prn) analgesic.
- Detoxification treatment of opioid addiction (heroin or other morphine-like drugs).
- Maintenance treatment of opioid addiction (heroin or other morphine-like drugs), in conjunction with appropriate social and medical services.

Limitations of Use

- Methadone products used for the treatment of opioid addiction in detoxification or maintenance programs are subject to the conditions for distribution and use required under 42 CFR 8.2.

Nucynta ER

Nucynta ER is indicated for the management of:

- Pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.
- Neuropathic pain associated with diabetic peripheral neuropathy (DPN) in adults severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

Limitations of Use

- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, reserve Nucynta ER for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.
- Nucynta ER is not indicated as an as-needed (prn) analgesic.

Opana ER

Opana ER is indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

Limitations of Use

- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, reserve Opana ER for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.
- Opana ER is not indicated as an as-needed (prn) analgesic.

OxyContin
Opioids ER - Step Therapy with MME Limit and Post Limit 2219-M 01-2019 (2) ©2019 CVS Caremark. All rights reserved.

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OxyContin is indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate in:
- Adults; and
- Opioid-tolerant pediatric patients 11 years of age and older who are already receiving and tolerate a minimum daily opioid dose of at least 20 mg oxycodone orally or its equivalent.

Limitations of Usage
- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, reserve OxyContin for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.
- OxyContin is not indicated as an as-needed (prn) analgesic.

Targiniq ER
Targiniq ER is indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

Limitations of Use
- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, reserve Targiniq ER for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.
- Targiniq ER is not indicated as an as-needed (prn) analgesic.

- The maximum total daily dose of Targiniq ER should not exceed 80 mg/40 mg (40 mg/20 mg q12h) because higher doses may be associated with symptoms of opioid withdrawal or decreased analgesia.

Troxyca ER
Troxyca ER is indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

Limitations of Use
- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, reserve Troxyca ER for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.
- Troxyca ER is not indicated as an as-needed (prn) analgesic.

Vantrela ER
Vantrela ER is an opioid agonist indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

Limitation of Use
- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, reserve Vantrela ER for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.
- Vantrela ER is not indicated as an as-needed (prn) analgesic.

Xtampza ER
Xtampza ER is indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

Limitations of Use
- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, reserve Xtampza ER for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.
- Xtampza ER is not indicated as an as-needed (prn) analgesic.

Zohydro ER
Zohydro ER is indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

Limitations of Use

- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, reserve Zohydro ER for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.
- Zohydro ER is not indicated as an as-needed (prn) analgesic.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for pain associated with cancer, sickle cell disease, a terminal condition, or pain being managed through hospice or palliative care

OR

- The requested drug is being prescribed for CHRONIC pain severe enough to require daily, around-the-clock, long-term treatment in a patient who has been taking an opioid [Note: Chronic pain is generally defined as pain that typically lasts greater than 3 months.]

AND

- The patient can safely take the requested dose based on their history of opioid use

AND

- The patient has been evaluated and the patient will be monitored regularly for the development of opioid use disorder

AND

- The patient’s pain will be reassessed in the first month after the initial prescription or any dose increase AND every 3 months thereafter to ensure that clinically meaningful improvement in pain and function outweigh risks to patient safety

AND

- This request is for continuation of therapy for a patient who has been receiving an extended-release opioid agent for at least 30 days OR

AND

- The patient has severe continuous pain and the patient has received an immediate-release opioid for at least one week

AND

- If the request is for a methadone product, then it is NOT being prescribed for detoxification treatment or as part of a maintenance treatment plan for opioid/substance abuse or addiction

[Note: These drugs should be prescribed only by healthcare professionals who are knowledgeable in the use of potent opioids for the management of chronic pain.]

Quantity Limits may apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Extended-release opioids are indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, reserve extended-release opioids for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain. Extended-release opioids are not indicated as as-needed (prn) analgesics. These drugs should be prescribed only by healthcare professionals who are knowledgeable in the use of potent opioids for the management of chronic pain."
If the patient has filled a prescription for at least a 1-day supply of a drug indicating the patient is being treated for cancer or sickle cell disease (SCD) within the past 365 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

If a claim is submitted with an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

If the patient has an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in their member health profile in the past 365 days, then the requested drug will be paid under that prescription benefit.

If a claim is submitted using a hospice patient residence code under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

For patients with no prescription claims of a cancer drug or a sickle cell disease drug in the past 365 days, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care submitted with their prescription claim, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in the member health profile in the past 365 days, or no hospice patient residence code submitted with their prescription claim:

If the patient has filled a prescription for at least a 7-day supply of an immediate-release (IR) opioid agent indicated for the management of pain within prescription claim history in the past 90 days under a prescription benefit administered by CVS Caremark, then the initial quantity limit criteria will apply (see Column A and Column B in the Opioid Analgesics ER Quantity Limits Chart below).

If the patient has filled a prescription for at least a 30-day supply of an extended-release (ER) opioid agent indicated for the management of pain within prescription claim history in the past 90 days under a prescription benefit administered by CVS Caremark, then the initial quantity limit criteria will apply (see Column A and Column B in the Opioid Analgesics ER Quantity Limits Chart below).

If the patient does not have at least a 7-day supply of an immediate-release opioid agent indicated for the management of pain OR at least a 30-day supply of an extended-release opioid agent indicated for the management of pain within prescription claim history in the past 90 days (i.e., the patient has not used an IR opioid prior to the ER opioid OR the patient is not already stable on an ER opioid), then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

The Centers for Disease Control and Prevention (CDC) Guideline for Prescribing Opioids for Chronic Pain provides recommendations for primary care clinicians who are prescribing opioids for chronic pain outside of active cancer treatment, sickle cell disease, palliative care, and end-of-life care. The National Comprehensive Cancer Network (NCCN) guidelines for Adult Cancer Pain recommend for continuous pain, it is appropriate to give pain medication on a regular schedule with supplemental doses for breakthrough pain. Add an extended-release or long-acting formulation to provide background analgesia for control of chronic persistent pain controlled on stable doses of short-acting opioids. When possible, use the same opioid for short-acting and extended-release forms. Allow rescue doses of short-acting opioids up to every 1 hour as needed. The NCCN Palliative Care pain management recommendation is to treat according to NCCN guidelines for adult cancer pain. For patients with no prescription claims of a cancer drug in the past 365 days, no ICD 10 diagnosis code indicating cancer or palliative care submitted with their prescription claim, no ICD 10 diagnosis code indicating cancer or palliative care in the member health profile in the past 365 days, or no hospice patient residence code submitted with their prescription claim who are identified through the prior authorization criteria as having cancer, a terminal condition, or pain being managed through hospice or palliative care, step therapy criteria and post limit quantities will not apply.

According to the National Heart, Lung, and Blood Institute’s (NHLBI) guidelines for Sickle Cell Disease (SCD), pain is the most common symptom of SCD. Pain can be acute, chronic, or an acute episode superimposed on chronic pain.
Recurrent acute pain crises (also known as vaso-occlusive crises) are the most common manifestation of SCD. Chronic pain is also one of the most common chronic complications of SCD. Pain management must be guided by patient report of severity. No biomarkers or imaging studies can validate pain or assess its severity. Medications used to treat SCD-related pain should be tailored to the individual. For pain that is not relieved by nonsteroidal anti-inflammatory drugs (NSAIDs) or other measures, either short-acting or long-acting opioids may be used to manage pain in SCD. For patients with no prescription claims of a sickle cell disease drug in the past 365 days, no ICD 10 diagnosis code indicating sickle cell disease submitted with their prescription claim, or no ICD 10 diagnosis code indicating sickle cell disease in the member health profile in the past 365 days who are identified through the prior authorization criteria as having sickle cell disease, step therapy criteria and post limit quantities will not apply.

The CDC Guideline for Prescribing Opioids for Chronic Pain states that for patients not already receiving opioids, clinicians should not initiate opioid treatment with extended-release opioids and should not prescribe extended-release opioids for intermittent use. Extended-release opioids should be reserved for severe, continuous pain and should be considered only for patients who have received immediate-release opioids daily for at least one week. The American Pain Society (APS) Chronic Pain guideline states that short-acting opioids are probably safer for initial therapy since they have a shorter half-life and may be associated with a lower risk of inadvertent overdose. Proposed benefits of transitioning to long-acting opioids with around-the-clock dosing include more consistent control of pain, improved adherence, and lower risk of addiction or abuse. In patients on around-the-clock chronic opioid therapy with breakthrough pain, clinicians may consider as-needed opioids.

Patients with chronic pain may need to be dosed on an around-the-clock basis rather than on an as needed basis. The American Pain Society (APS) Chronic Pain guideline states that short-acting opioids are probably safer for initial therapy since they have a shorter half-life and may be associated with a lower risk of inadvertent overdose. Proposed benefits of transitioning to long-acting opioids with around-the-clock dosing include more consistent control of pain, improved adherence, and lower risk of addiction or abuse. In patients on around-the-clock chronic opioid therapy with breakthrough pain, clinicians may consider as-needed opioids.

Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.

Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should consider history of overdose, history of substance use disorder, higher opioid dosages (≥50 morphine milligram equivalents per day (MME/day)), or concurrent benzodiazepine use.

The CDC Guideline for Prescribing Opioids for Chronic Pain recommends that when opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when increasing dosage to ≥50 MME/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day. The extended-release opioid drug initial quantity limits are set to encompass the usual/starting dosage and frequency range recommendations in labeling without exceeding a monthly quantity that corresponds to 90 MME/day. If the patient is requesting more than the initial quantity limit, then the system will reject with a message indicating that a prior authorization is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

The American Pain Society Opioid Treatment Guidelines state that a reasonable definition for high dose opioid therapy is >200 mg daily of oral morphine (or equivalent). The extended-release opioid drug post limit quantities for approval are set to encompass the usual dosage and frequency range recommendations in labeling, or up to one additional dose per day above the initial quantity limit without exceeding a monthly quantity that corresponds to 200 MME per day (unless minimum FDA-labeled strength/dose/frequency exceeds a monthly quantity that corresponds to 200 MME/day) to promote optimization of pain management, safe and effective use, and to reduce misuse, abuse, and overdose.

Methadone products, when used for the treatment of opioid addiction in detoxification or maintenance programs, shall be dispensed only by opioid treatment programs (and agencies, practitioners or institutions by formal agreement with the program sponsor) certified by the Substance Abuse and Mental Health Services Administration and approved by the designated state authority. Certified treatment programs shall dispense and use methadone in oral form only and
The limit is set to reflect the use of methadone for the relief of pain. The limit is not intended for patients in detoxification and methadone maintenance programs. A separate initial quantity limit prior authorization criteria exists for methadone concentrate and dispersible tablets since they are indicated for opioid dependence only.

**PROGRAM DESCRIPTION**

Neither step therapy requirements nor quantity limits apply if the patient has a drug in claims history in the past year that indicates the patient is being treated for cancer or sickle cell disease. In addition, neither acute pain duration limits nor quantity limits will apply if a prescription claim is submitted with an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care, if the patient has an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in their member health profile in the past 365 days, or if a prescription claim is submitted using a hospice patient residence code.

**Step Therapy**

If a patient has filled at least a 7-day supply of an immediate-release (IR) opioid agent indicated for the management of pain within prescription claim history in the past 90 days OR has been receiving an extended-release (ER) opioid agent indicated for the management of pain for at least a 30 days within prescription claim history in the past 90 days, then the extended-release opioid will adjudicate for up to the initial quantity limit.

If the patient does not have at least a 7-day supply of an immediate-release opioid agent indicated for the management of pain OR at least a 30-day supply of an extended-release opioid agent indicated for the management of pain within prescription claim history in the past 90 days (i.e., the patient has not used an IR opioid prior to the ER opioid OR the patient is not already stable on an ER opioid), then the claim will reject with a message indicating that a prior authorization (PA) is required. For patients with no prescription claims of a cancer drug or a sickle cell disease drug in the past 365 days, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care submitted with their prescription claim, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in the member health profile in the past 365 days, or no hospice patient residence code submitted with their prescription claim who are identified through the prior authorization criteria as having cancer, sickle cell disease, a terminal condition, or pain being managed through hospice or palliative care, step therapy requirements will not apply.

**Quantity Limit/Post Limit**

Plans implementing morphine milligram equivalent (MME)-based quantity limits on extended-release opioids are providing coverage for an initial amount of a monthly quantity that corresponds to 90 MME or less per day. Coverage is provided for up to the initial quantity limit per Column A and Column B in the Opioid Analgesics ER Quantity Limits Chart below.

Prior authorization review is required to determine coverage for additional quantities above the initial limit.

Post limit quantities are set not to exceed a monthly quantity that corresponds to 200 MME/day (unless minimum FDA-labeled strength/dose/frequency exceeds a monthly quantity that corresponds to 200 MME/day). For patients with no prescription claims of a cancer drug or a sickle cell disease drug in the past 365 days, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care submitted with their prescription claim, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in the member health profile in the past 365 days, or no hospice patient residence code submitted with their prescription claim who are identified through the prior authorization criteria as having cancer, sickle cell disease, a terminal condition, or pain being managed through hospice or palliative care, post limit quantities will not apply.

*Step Therapy logic will apply first, followed by initial quantity limit logic.*

**REFERENCES**

INITIAL STEP THERAPY
If the patient has filled a prescription for at least a 1-day supply of a drug indicating the patient is being treated for cancer or sickle cell disease within the past 365 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

If a claim is submitted with an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

If the patient has an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in their member health profile in the past 365 days, then the requested drug will be paid under that prescription benefit.

If a claim is submitted using a hospice patient residence code under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

For patients with no prescription claims of a cancer drug or a sickle cell disease drug in the past 365 days, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care submitted with their prescription claim, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in the member health profile in the past 365 days, or no hospice patient residence code submitted with their prescription claim:
If the patient has filled a prescription for at least a 7-day supply of an immediate-release (IR) opioid agent indicated for the management of pain within prescription claim history in the past 90 days under a prescription benefit administered by CVS Caremark, then the initial quantity limit criteria will apply (see Column A and Column B in the Opioid Analgesics ER Quantity Limits Chart below).

If the patient has filled a prescription for at least a 30-day supply of an extended-release (ER) opioid agent indicated for the management of pain within prescription claim history in the past 90 days under a prescription benefit administered by CVS Caremark, then the initial quantity limit criteria will apply (see Column A and Column B in the Opioid Analgesics ER Quantity Limits Chart below).

If the patient does not have at least a 7-day supply of an immediate-release opioid agent indicated for the management of pain OR at least a 30-day supply of an extended-release opioid agent indicated for the management of pain within prescription claim history in the past 90 days (i.e., the patient has not used an IR opioid prior to the ER opioid OR the patient is not already stable on an ER opioid), then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

CRITERIA FOR APPROVAL

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<table>
<thead>
<tr>
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<tbody>
<tr>
<td>1</td>
<td>Is the requested drug being prescribed for pain associated with cancer, sickle cell disease, a terminal condition, or pain being managed through hospice or palliative care? [If yes, then no further questions.]</td>
</tr>
<tr>
<td>2</td>
<td>Is the requested drug being prescribed for CHRONIC pain severe enough to require daily, around-the-clock, long-term treatment in a patient who has been taking an opioid? [Note: Chronic pain is generally defined as pain that typically lasts greater than 3 months.]</td>
</tr>
<tr>
<td>3</td>
<td>Can the patient safely take the requested dose based on their history of opioid use?</td>
</tr>
<tr>
<td>4</td>
<td>Has the patient been evaluated and will the patient be monitored regularly for the development</td>
</tr>
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</table>
of opioid use disorder?

5 Will the patient’s pain be reassessed in the first month after the initial prescription or any dose increase AND every 3 months thereafter to ensure that clinically meaningful improvement in pain and function outweigh risks to patient safety?  

| Yes | No |

6 Is this request for continuation of therapy for a patient who has been receiving an extended-release opioid agent for at least 30 days?  
[If yes, then skip to question 8.]

| Yes | No |

7 Does the patient have severe continuous pain and has the patient received an immediate-release opioid for at least one week?  

| Yes | No |

8 Which drug is being requested? Please check the drug being requested.  
[Note: These drugs should be prescribed only by healthcare professionals who are knowledgeable in the use of potent opioids for the management of chronic pain.]

- [ ] Arymo ER (morphine extended-release tablets) (if checked, go to 20)
- [ ] Avinza (morphine extended-release capsules) (if checked, go to 12)
- [ ] Belbuca (buprenorphine buccal film) (if checked, go to 13)
- [ ] Butrans (buprenorphine transdermal system) (if checked, go to 14)
- [ ] Conzip (tramadol hydrochloride extended-release) (if checked, go to 15)
- [ ] Dolophine 5 mg, 10 mg (methadone hydrochloride tablets) (if checked, go to 10)
- [ ] Duragesic (fentanyl transdermal system) (if checked, go to question 16)
- [ ] Embeda (morphine sulfate/naltrexone HCl extended-release) (if checked, go to question 17)
- [ ] Exalgo (hydromorphone hydrochloride extended-release tabs) (if checked, go to question 18)
- [ ] Hysingla ER (hydrocodone bitartrate extended-release tablets) (if checked, go to 9)
- [ ] Kadian (morphine extended-release capsules) (if checked, go to question 19)
- [ ] Methadone 10 mg/mL Intensol soln (if checked, go to 10)
- [ ] Methadone 5 mg/5 mL, 10 mg/5 mL oral soln, 200 mg/20 mL injection (if checked, go to 10)
- [ ] Methadone 5 mg, 10 mg (methadone hydrochloride tablets) (if checked, go to 10)
- [ ] MorphaBond ER (morphine extended-release tablets) (if checked, go to question 20)
- [ ] MS Contin (morphine extended-release tablets) (if checked, go to 20)
- [ ] Nucynta ER (tapentadol extended-release tablets) (if checked, go to 21)
- [ ] Opana ER (oxymorphone hydrochloride extended-release tablets) (if checked, go to 22)
- [ ] OxyContin (oxycodone hydrochloride extended-release tablets) (if checked, go to 23)
- [ ] Targiniq ER (oxycodone HCl/naloxone HCl extended-release tablets) (if checked, go to 24)
- [ ] Tramadol hydrochloride extended-release (if checked, go to 15)
- [ ] Ultram ER (tramadol hydrochloride extended-release tablets) (if checked, go to 15)
- [ ] VanTrela ER (hydrocodone bitartrate extended-release tablets) (if checked, go to 9)
- [ ] Xtampza ER (oxycodone extended-release capsules) (if checked, go to 25)
- [ ] Zohydro ER (hydrocodone bitartrate extended-release capsules) (if checked, go to 9)
- [ ] Troxyca ER (oxycodone/naltrexone extended-release capsules) (if checked, go to 26)

9 Does the patient require use of MORE than the plan allowance PER MONTH of any of the following: A) 90 units of Zohydro ER 10 mg, 15 mg, 20 mg, 30 mg, 40 mg OR VanTrela ER 15 mg, 30 mg, 45 mg, B) 60 units of Hysingla ER 20 mg, 30 mg, 40 mg, 60 mg, 80 mg, 100 mg OR Zohydro ER 50 mg OR VanTrela ER 60 mg, 90 mg, C) 30 units of Hysingla ER 120 mg?  

[No further questions.]

[RPh Note: If yes, then deny and enter a partial approval for ONE of the following: A) 90]
10 Is the requested methadone product being prescribed for detoxification treatment or as part of a maintenance treatment plan for opioid/substance abuse or addiction?  

Yes  No

11 Does the patient require use of MORE than the plan allowance PER MONTH of any of the following: A) 120 tablets of Dolophine 5 mg or Methadone 5 mg, B) 90 tablets of Dolophine 10 mg or Methadone 10 mg, C) 600 mL of Methadone 5 mg/5 mL oral solution, D) 450 mL of Methadone 10 mg/5 mL oral solution, E) 40 mL (2 multidose vials) of Methadone 200 mg/20 mL injection, F) 90 mL of Methadone 10 mg/mL Intensol solution?  

[No further questions.]  

[RPh Note: If yes, then deny and enter a partial approval for ONE of the following: A) 120 tablets/month of Dolophine 5 mg or Methadone 5 mg, B) 90 tablets/month of Dolophine 10 mg or Methadone 10 mg, C) 600 mL/month of Methadone 5 mg/5 mL oral solution, D) 450 mL/month of Methadone 10 mg/5 mL oral solution, E) 40 mL (2 multidose vials) of Methadone 200 mg/20 mL injection, F) 90 mL/month of Methadone 10 mg/mL Intensol solution.]  

Yes  No

12 Does the patient require use of MORE than the plan allowance PER MONTH of 60 capsules of Avinza 30 mg, 45 mg, 60 mg, 75 mg, 90 mg OR MORE than the plan allowance PER MONTH of 30 capsules of Avinza 120 mg?  

[No further questions.]  

[RPh Note: If yes, then deny and enter a partial approval for 60 capsules/month of Avinza 30 mg, 45 mg, 60 mg, 75 mg, 90 mg OR 30 capsules/month of Avinza 120 mg.]  

Yes  No

13 Does the patient require use of MORE than the plan allowance PER MONTH of 90 films of Belbuca 75 mcg, 150 mcg, 300 mcg, 450 mcg OR MORE than the plan allowance PER MONTH of 60 films of Belbuca 600 mcg, 750 mcg, 900 mcg?  

[No further questions.]  

[RPh Note: If yes, then deny and enter a partial approval for 90 films/month of Belbuca 75 mcg, 150 mcg, 300 mcg, 450 mcg OR 60 films per month of Belbuca 600 mcg, 750 mcg, 900 mcg.]  

Yes  No

14 Does the patient require use of MORE than the plan allowance PER MONTH of 8 patches of Butrans 5 mcg/hr, 7.5 mcg/hr, 10 mcg/hr OR MORE than the plan allowance PER MONTH of 4 patches of Butrans 15 mcg/hr, 20 mcg/hr?  

[No further questions.]  

[RPh Note: If yes, then deny and enter a partial approval for 8 patches/month of Butrans 5 mcg/hr, 7.5 mcg/hr, 10 mcg/hr OR 4 patches/month of Butrans 15 mcg/hr, 20 mcg/hr.]  

Yes  No

15 Does the patient require use of MORE than the plan allowance PER MONTH of 60 units of Conzip 100 mg, tramadol ER 100 mg, 150 mg, or Ultram ER 100 mg, OR MORE than the plan allowance PER MONTH of 30 units of Conzip 200 mg, 300 mg, or tramadol ER 200 mg, 300 mg, or Ultram ER 200 mg, 300 mg?  

[No further questions.]  

Yes  No
16 Does the patient require use of MORE than the plan allowance PER MONTH of 20 patches of Duragesic 12 mcg/hr, 25 mcg/hr, 37.5 mcg/hr OR MORE than the plan allowance PER MONTH of 10 patches of Duragesic 50 mcg/hr, 62.5 mcg/hr, 75 mcg/hr, 87.5 mcg/hr, 100 mcg/hr?

[No further questions.]

17 Does the patient require use of MORE than the plan allowance PER MONTH of 90 capsules of Embeda 20 mg/0.8 mg, 30 mg/1.2 mg OR MORE than the plan allowance PER MONTH of 60 capsules of Embeda 50 mg/2 mg, 60 mg/2.4 mg, 80 mg/3.2 mg, 100 mg/4 mg?

[No further questions.]

18 Does the patient require use of MORE than the plan allowance PER MONTH of 60 tablets of Exalgo 8 mg, 12 mg, 16 mg OR MORE than the plan allowance PER MONTH of 30 tablets of Exalgo 32 mg?

[No further questions.]

19 Does the patient require use of MORE than the plan allowance PER MONTH of any of the following: A) 90 capsules of Kadian 10 mg, 20 mg, 30 mg, 40 mg, B) 60 capsules of Kadian 50 mg, 60 mg, 70 mg, 80 mg, 100 mg, C) 30 capsules of Kadian 130 mg, 150 mg, 200 mg?

[No further questions.]

20 Does the patient require use of MORE than the plan allowance PER MONTH of any of the following: A) 120 tablets of Arymo ER 15 mg, 30 mg or MorphaBond ER 15 mg, 30 mg or MS Contin 15 mg, 30 mg, B) 90 tablets of Arymo ER 60 mg or MorphaBond ER 60 mg or MS Contin 60 mg, C) 60 tablets of MorphaBond ER 100 mg or MS Contin 100 mg, 200 mg?

[No further questions.]
21 Does the patient require use of MORE than the plan allowance PER MONTH of 90 tablets of Nucynta ER 50 mg, 100 mg, 150 mg OR MORE than the plan allowance PER MONTH of 60 tablets of Nucynta ER 200 mg, 250 mg?  
[No further questions.]  
[Ph Note: If yes, then deny and enter a partial approval for 90 tablets/month of Nucynta ER 50 mg, 100 mg, 150 mg OR 60 tablets/month of Nucynta ER 200 mg, 250 mg.]

22 Does the patient require use of MORE than the plan allowance PER MONTH of 90 tablets of Opana ER 5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg, OR MORE than the plan allowance PER MONTH of 60 tablets of Opana ER 30 mg, 40 mg?  
[No further questions.]  
[Ph Note: If yes, then deny and enter a partial approval for 90 tablets/month of Opana ER 5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg, OR 60 tablets/month of Opana ER 30 mg, 40 mg.]

23 Does the patient require use of MORE than the plan allowance PER MONTH of 90 tablets of OxyContin 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, OR MORE than the plan allowance PER MONTH of 60 tablets of OxyContin 60 mg, 80 mg?  
[No further questions.]  
[Ph Note: If yes, then deny and enter a partial approval for 90 tablets/month of OxyContin 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, OR 60 tablets/month of OxyContin 60 mg, 80 mg.]

24 Does the patient require use of MORE than the plan allowance PER MONTH of 90 tablets of Targiniq ER 10 mg/5 mg, 20 mg/10 mg OR MORE than the plan allowance PER MONTH of 60 tablets of Targiniq ER 40 mg/20 mg?  
[No further questions.]  
[Ph Note: If yes, then deny and enter a partial approval for 90 tablets/month of Targiniq ER 10 mg/5 mg, 20 mg/10 mg OR 60 tablets/month of Targiniq ER 40 mg/20 mg.]

25 Does the patient require use of MORE than the plan allowance PER MONTH of 90 capsules of Xtampza ER?  
[No further questions.]  
[Ph Note: If yes, then deny and enter a partial approval for 90 capsules/month of Xtampza ER.]

26 Does the patient require use of MORE than the plan allowance PER MONTH of 90 capsules of Troxyca ER 10 mg/1.2 mg, 20 mg/2.4 mg, 30 mg/3.6 mg, 40 mg/4.8 mg OR MORE than the plan allowance PER MONTH of 60 capsules of Troxyca ER 60 mg/7.2 mg, 80 mg/9.6 mg?  
[Ph Note: If yes, then deny and enter a partial approval for 90 capsules/month of Troxyca ER 10 mg/1.2 mg, 20 mg/2.4 mg, 30 mg/3.6 mg, 40 mg/4.8 mg OR 60 capsules/month of Troxyca ER 60 mg/7.2 mg, 80 mg/9.6 mg.]

<table>
<thead>
<tr>
<th>Mapping Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>YES</strong></td>
</tr>
<tr>
<td>1. Approve, 12 months,</td>
</tr>
</tbody>
</table>

Opioids ER - Step Therapy with MME Limit and Post Limit 2219-M 01-2019 (2) 
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<table>
<thead>
<tr>
<th>Step</th>
<th>Description</th>
<th>Decision</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.</td>
<td>Go to 3</td>
<td>Deny</td>
</tr>
<tr>
<td>3.</td>
<td>Go to 4</td>
<td>Deny</td>
</tr>
<tr>
<td>4.</td>
<td>Go to 5</td>
<td>Deny</td>
</tr>
<tr>
<td>5.</td>
<td>Go to 6</td>
<td>Deny</td>
</tr>
<tr>
<td>6.</td>
<td>Go to 8</td>
<td>Go to 7</td>
</tr>
<tr>
<td>7.</td>
<td>Go to 8</td>
<td>Deny</td>
</tr>
<tr>
<td>8.</td>
<td>N/A</td>
<td></td>
</tr>
</tbody>
</table>

You do not meet the requirements of your plan. Your plan covers this drug when you meet one of the following conditions:
- You have been taking an opioid and you are using the drug for chronic pain that is severe enough that you need daily, around-the-clock, long-term treatment
- You have pain due to cancer, sickle cell disease, or a terminal condition
- Your pain is being managed through hospice or palliative care

Your request has been denied based on the information we have.

[Short Description: No approvable diagnosis.]

You do not meet the requirements of your plan. Your plan covers this drug when you can safely take the drug based on your history of opioid use. Your request has been denied based on the information we have.

[Short Description: Patient cannot safely take requested dose.]

You do not meet the requirements of your plan. Your plan covers this drug when you will be monitored regularly. Your request has been denied based on the information we have.

[Short Description: Patient not monitored regularly for opioid use disorder.]

You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions:
- Your pain will be checked the first month after your initial prescription or after a dose increase and every 3 months after that
- The benefits outweigh the risks of taking the medication

Your request has been denied based on the information we have.

[Short Description: Patient’s pain is not being reassessed.]

You do not meet the requirements of your plan. Your plan covers this drug when you have one of these conditions:
- You have already been taking an extended-release opioid drug for 30 days
- You have severe continuous pain and tried immediate-release opioids for one week

Your request has been denied based on the information we have.

[Short Description: No 30-day ER or 7-day IR opioid in history.]
### 9. Deny

**RPh Note:** For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.

<table>
<thead>
<tr>
<th>Quantity Limits Chart (Column C for 1 month supply or Column D for a 3 month supply)</th>
</tr>
</thead>
<tbody>
<tr>
<td>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:</td>
</tr>
<tr>
<td>- 90 units/month of Zohydro ER 10 mg, 15 mg, 20 mg, 30 mg, 40 mg OR Vantrela ER 15 mg, 30 mg, 45 mg</td>
</tr>
<tr>
<td>- 60 units/month of Hysingla ER 20 mg, 30 mg, 40 mg, 60 mg, 80 mg, 100 mg OR Zohydro ER 50 mg OR Vantrela ER 60 mg, 90 mg</td>
</tr>
<tr>
<td>- 30 units/month of Hysingla ER 120 mg</td>
</tr>
<tr>
<td>You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.</td>
</tr>
</tbody>
</table>

[Short Description: Over max quantity.]

### 10. Deny

| Go to 11 |
| You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: |
| - You are using the drug for pain that is severe enough that you need daily, around-the-clock, long-term treatment |
| - You are not using the drug for detoxification treatment |
| - You are not using the drug as part of a treatment plan for opioid/substance abuse or addiction |
| Your request has been denied based on the information we have. |

[Short Description: Should not be used for opioid/substance abuse or addiction.]

### 11. Deny

**RPh Note:** For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.

<table>
<thead>
<tr>
<th>Quantity Limits Chart (Column C for 1 month supply or Column D for a 3 month supply)</th>
</tr>
</thead>
<tbody>
<tr>
<td>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:</td>
</tr>
<tr>
<td>- 120 tablets/month of Dolophine 5 mg or Methadone 5 mg</td>
</tr>
<tr>
<td>- 90 tablets/month of Dolophine 10 mg or Methadone 10 mg</td>
</tr>
<tr>
<td>- 600 mL/month of Methadone 5 mg/5 mL oral solution</td>
</tr>
<tr>
<td>- 450 mL/month of Methadone 10 mg/5 mL oral solution</td>
</tr>
<tr>
<td>- 40 mL (2 multidose vials) of Methadone 200 mg/20 mL injection</td>
</tr>
<tr>
<td>- 90 mL/month of Methadone 10 mg/mL Intensol solution</td>
</tr>
<tr>
<td>You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.</td>
</tr>
</tbody>
</table>

[Short Description: Over max quantity.]

### 12. Deny

**RPh Note:** For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.

<table>
<thead>
<tr>
<th>Quantity Limits Chart (Column C for 1 month supply or Column D for a 3 month supply)</th>
</tr>
</thead>
<tbody>
<tr>
<td>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:</td>
</tr>
<tr>
<td>- 60 capsules/month of Avinza 30 mg, 45 mg, 60 mg, 75 mg, 90 mg</td>
</tr>
<tr>
<td>- 30 capsules/month of Avinza 120 mg</td>
</tr>
<tr>
<td>You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.</td>
</tr>
</tbody>
</table>

[Short Description: Over max quantity.]
<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>13.</td>
<td>Deny</td>
<td>Approve, 12 months</td>
</tr>
<tr>
<td>RPh Note: For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.</td>
<td>See Opioid Analgesics ER Quantity Limits Chart (Column C for 1 month supply or Column D for a 3 month supply)</td>
<td></td>
</tr>
<tr>
<td>14.</td>
<td>Deny</td>
<td>Approve, 12 months</td>
</tr>
<tr>
<td>RPh Note: For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.</td>
<td>See Opioid Analgesics ER Quantity Limits Chart (Column C for 1 month supply or Column D for a 3 month supply)</td>
<td></td>
</tr>
<tr>
<td>15.</td>
<td>Deny</td>
<td>Approve, 12 months</td>
</tr>
<tr>
<td>RPh Note: For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.</td>
<td>See Opioid Analgesics ER Quantity Limits Chart (Column C for 1 month supply or Column D for a 3 month supply)</td>
<td></td>
</tr>
<tr>
<td>16.</td>
<td>Deny</td>
<td>Approve, 12 months</td>
</tr>
<tr>
<td>RPh Note: For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.</td>
<td>See Opioid Analgesics ER Quantity Limits Chart (Column C for 1 month supply or Column D for a 3 month supply)</td>
<td></td>
</tr>
<tr>
<td>17.</td>
<td>Deny</td>
<td>Approve, 12 months</td>
</tr>
<tr>
<td>Number</td>
<td>Deny RPh Note: For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.</td>
<td>Approve, 12 months</td>
</tr>
<tr>
<td>--------</td>
<td>-------------------------------------------------------------------------------------------------</td>
<td>-----------------</td>
</tr>
<tr>
<td>18.</td>
<td>See Opioid Analgesics ER Quantity Limits Chart (Column C for 1 month supply or Column D for a 3 month supply)</td>
<td>You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.</td>
</tr>
<tr>
<td>19.</td>
<td>See Opioid Analgesics ER Quantity Limits Chart (Column C for 1 month supply or Column D for a 3 month supply)</td>
<td>You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.</td>
</tr>
<tr>
<td>20.</td>
<td>See Opioid Analgesics ER Quantity Limits Chart (Column C for 1 month supply or Column D for a 3 month supply)</td>
<td>You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.</td>
</tr>
<tr>
<td>21.</td>
<td>See Opioid Analgesics ER Quantity Limits Chart (Column C for 1 month supply or Column D for a 3 month supply)</td>
<td>You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.</td>
</tr>
</tbody>
</table>

- 90 capsules/month of Embeda 20/0.8 mg or 30/1.2 mg
- 60 capsules/month of Embeda 50/2 mg, 60/2.4 mg, 80/3.2 mg, or 100/4 mg

You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.

[Short Description: Over max quantity.]
<table>
<thead>
<tr>
<th>Requested Drug</th>
<th>Quantity Limits Chart (Column C for 1 month supply or Column D for a 3 month supply)</th>
<th>Deny Reason</th>
</tr>
</thead>
</table>
| **22.** | You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:  
- 90 tablets/month of Opana ER 5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg  
- 60 tablets/month of Opana ER, 30 mg, 40 mg  
You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.  
[Short Description: Over max quantity.] |
| **23.** | You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:  
- 90 tablets/month of OxyContin 10 mg, 15 mg, 20 mg, 30 mg, 40 mg  
- 60 tablets/month of OxyContin 60 mg, 80 mg  
You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.  
[Short Description: Over max quantity.] |
| **24.** | You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:  
- 90 tablets/month of Targiniq ER 10 mg/5 mg, 20 mg/10 mg  
- 60 tablets/month of Targiniq ER 40 mg/20 mg  
You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.  
[Short Description: Over max quantity.] |
| **25.** | You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 90 capsules/month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.  
[Short Description: Over max quantity.] |
You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:
- 90 capsules/month of Troxyca ER 10 mg/1.2 mg, 20 mg/2.4 mg, 30 mg/3.6 mg, 40 mg/4.8 mg
- 60 capsules/month of Troxyca ER 60 mg/7.2 mg, 80 mg/9.6 mg
You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.

[Short Description: Over max quantity.]
<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>MME Limit</th>
<th>Post Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avinza 60 mg</td>
<td>q24h, MAX 1600 mg/day</td>
<td>90 caps (60 MME/day)</td>
<td>60 caps (120 MME/day)</td>
</tr>
<tr>
<td>Avinza 75 mg</td>
<td>q24h, MAX 1600 mg/day</td>
<td>90 caps (75 MME/day)</td>
<td>60 caps (150 MME/day)</td>
</tr>
<tr>
<td>Avinza 90 mg</td>
<td>q24h, MAX 1600 mg/day</td>
<td>90 caps (90 MME/day)</td>
<td>60 caps (180 MME/day)</td>
</tr>
<tr>
<td>Avinza 120 mg</td>
<td>q24h, MAX 1600 mg/day</td>
<td>0***</td>
<td>30 caps (120 MME/day)</td>
</tr>
<tr>
<td>Belbuca 75 mcg</td>
<td>q12h, MAX 900 mcg/12 hrs</td>
<td>60 films (4.5 MME/day)</td>
<td>90 films (6.75 MME/day)</td>
</tr>
<tr>
<td>Belbuca 150 mcg</td>
<td>q12h, MAX 900 mcg/12 hrs</td>
<td>60 films (9 MME/day)</td>
<td>90 films (13.5 MME/day)</td>
</tr>
<tr>
<td>Belbuca 300 mcg</td>
<td>q12h, MAX 900 mcg/12 hrs</td>
<td>60 films (18 MME/day)</td>
<td>90 films (27 MME/day)</td>
</tr>
<tr>
<td>Belbuca 450 mcg</td>
<td>q12h, MAX 900 mcg/12 hrs</td>
<td>60 films (27 MME/day)</td>
<td>90 films (40.5 MME/day)</td>
</tr>
<tr>
<td>Belbuca 600 mcg</td>
<td>q12h, MAX 900 mcg/12 hrs</td>
<td>0***</td>
<td>60 films (36 MME/day)</td>
</tr>
<tr>
<td>Belbuca 750 mcg</td>
<td>q12h, MAX 900 mcg/12 hrs</td>
<td>0***</td>
<td>60 films (45 MME/day)</td>
</tr>
<tr>
<td>Belbuca 900 mcg</td>
<td>q12h, MAX 900 mcg/12 hrs</td>
<td>0***</td>
<td>60 films (54 MME/day)</td>
</tr>
<tr>
<td>Butrans 5 mcg/hr</td>
<td>q7d, MAX 20 mcg/hr</td>
<td>4 patches (9 MME/day)</td>
<td>8 patches (18 MME/day)</td>
</tr>
<tr>
<td>Butrans 7.5 mcg/hr</td>
<td>q7d, MAX 20 mcg/hr</td>
<td>4 patches (13.5 MME/day)</td>
<td>8 patches (27 MME/day)</td>
</tr>
<tr>
<td>Butrans 10 mcg/hr</td>
<td>q7d, MAX 20 mcg/hr</td>
<td>4 patches (18 MME/day)</td>
<td>8 patches (36 MME/day)</td>
</tr>
<tr>
<td>Butrans 15 mcg/hr</td>
<td>q7d, MAX 20 mcg/hr</td>
<td>0***</td>
<td>4 patches (27 MME/day)</td>
</tr>
<tr>
<td>Butrans 20 mcg/hr</td>
<td>q7d, MAX 20 mcg/hr</td>
<td>0***</td>
<td>4 patches (36 MME/day)</td>
</tr>
<tr>
<td>Conzip 100 mg</td>
<td>qd, MAX 300 mg/day</td>
<td>30 caps (10 MME/day)</td>
<td>60 caps (20 MME/day)</td>
</tr>
<tr>
<td>Conzip 200 mg</td>
<td>qd, MAX 300 mg/day</td>
<td>0***</td>
<td>30 caps (20 MME/day)</td>
</tr>
<tr>
<td>Conzip 300 mg</td>
<td>qd, MAX 300 mg/day</td>
<td>0***</td>
<td>30 caps (30 MME/day)</td>
</tr>
<tr>
<td>Dolophine 5 mg</td>
<td>q8-12h</td>
<td>90 tabs (60 MME/day)</td>
<td>120 tabs (80 MME/day)</td>
</tr>
<tr>
<td>Dolophine 10 mg</td>
<td>q8-12h</td>
<td>60 tabs (80 MME/day)</td>
<td>90 tabs (120 MME/day)</td>
</tr>
<tr>
<td>Duragesic 12 mcg/hr</td>
<td>q72h</td>
<td>10 patches (28.8 MME/day)</td>
<td>20 patches (57.6 MME/day)</td>
</tr>
<tr>
<td>Duragesic 25 mcg/hr</td>
<td>q72h</td>
<td>10 patches (60 MME/day)</td>
<td>20 patches (120 MME/day)</td>
</tr>
<tr>
<td>Duragesic 37.5 mcg/hr</td>
<td>q72h</td>
<td>10 patches (90 MME/day)</td>
<td>20 patches (180 MME/day)</td>
</tr>
<tr>
<td>Duragesic 50 mcg/hr</td>
<td>q72h</td>
<td>0***</td>
<td>10 patches (120 MME/day)</td>
</tr>
<tr>
<td>Duragesic 62.5 mcg/hr</td>
<td>q72h</td>
<td>0***</td>
<td>10 patches (150 MME/day)</td>
</tr>
<tr>
<td>Duragesic 75 mcg/hr</td>
<td>q72h</td>
<td>0***</td>
<td>10 patches (180 MME/day)</td>
</tr>
<tr>
<td>Duragesic 87.5 mcg/hr</td>
<td>q72h</td>
<td>0***</td>
<td>10 patches (210 MME/day)</td>
</tr>
<tr>
<td>Duragesic 100 mcg/hr</td>
<td>q72h</td>
<td>0***</td>
<td>10 patches (240 MME/day)</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Drug</th>
<th>Formulation</th>
<th>MME Limit</th>
<th>Dose Limit</th>
<th>Days Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Embeda 20 mg/0.8 mg</td>
<td>q12-24h</td>
<td>60 caps (40 MME/day)</td>
<td>180 caps (40 MME/day)</td>
<td>90 caps (60 MME/day)</td>
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<tr>
<td>Embeda 30 mg/1.2 mg</td>
<td>q12-24h</td>
<td>60 caps (60 MME/day)</td>
<td>180 caps (60 MME/day)</td>
<td>90 caps (90 MME/day)</td>
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<td>Embeda 50 mg/2 mg</td>
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<td>60 caps (100 MME/day)</td>
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<td>30 caps (60 MME/day)</td>
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<td>60 caps (120 MME/day)</td>
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<td>60 caps (160 MME/day)</td>
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<td>Embeda 100 mg/4 mg</td>
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<td>0***</td>
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<tr>
<td>Exalgo 8 mg</td>
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<td>90 tabs (64 MME/day)</td>
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<tr>
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<td>0***</td>
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<td>Hysingla ER 20 mg</td>
<td>q24h</td>
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<td>90 tabs (20 MME/day)</td>
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<tr>
<td>Hysingla ER 30 mg</td>
<td>q24h</td>
<td>30 tabs (30 MME/day)</td>
<td>90 tabs (30 MME/day)</td>
<td>60 tabs (60 MME/day)</td>
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<td>Hysingla ER 40 mg</td>
<td>q24h</td>
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<td>90 tabs (40 MME/day)</td>
<td>60 tabs (80 MME/day)</td>
</tr>
<tr>
<td>Hysingla ER 60 mg</td>
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<td>90 tabs (60 MME/day)</td>
<td>60 tabs (120 MME/day)</td>
</tr>
<tr>
<td>Hysingla ER 80 mg</td>
<td>q24h</td>
<td>30 tabs (80 MME/day)</td>
<td>90 tabs (80 MME/day)</td>
<td>60 tabs (160 MME/day)</td>
</tr>
<tr>
<td>Hysingla ER 100 mg</td>
<td>q24h</td>
<td>0***</td>
<td>0***</td>
<td>60 tabs (200 MME/day)</td>
</tr>
<tr>
<td>Kadian 10 mg</td>
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<td>180 caps (20 MME/day)</td>
<td>90 caps (30 MME/day)</td>
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<td>Kadian 20 mg</td>
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<tr>
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<td>90 caps (60 MME/day)</td>
<td>60 caps (120 MME/day)</td>
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<td>Kadian 70 mg</td>
<td>q12-24h</td>
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<td>Kadian 80 mg</td>
<td>q12-24h</td>
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<td>90 caps (80 MME/day)</td>
<td>60 caps (160 MME/day)</td>
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<tr>
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<td>0***</td>
<td>0***</td>
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<tr>
<td>Kadian 130 mg</td>
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<td>Kadian 150 mg</td>
<td>q12-24h</td>
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<td>0***</td>
<td>30 caps (150 MME/day)</td>
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<tr>
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<td>q12-24h</td>
<td>0***</td>
<td>0***</td>
<td>30 caps (200 MME/day)</td>
</tr>
<tr>
<td>Methadone 5 mg</td>
<td>q8-12h</td>
<td>90 tabs</td>
<td>270 tabs</td>
<td>120 tabs</td>
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<tr>
<td>Opioid</td>
<td>Dosage Form</td>
<td>MME Limit</td>
<td>Dose/Day</td>
<td>MME/Day</td>
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<td>---------------------</td>
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<tr>
<td>Methadone 10 mg</td>
<td>q8-12h</td>
<td>(60 MME/day)</td>
<td>60 tabs (80 MME/day)</td>
<td>180 tabs (80 MME/day)</td>
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<td>Methadone 200 mg/20 mL injection</td>
<td>q8-12h</td>
<td>(1 multidose vial) (26.7 MME/day)</td>
<td>60 mL (3 multidose vials) (26.7 MME/day)</td>
<td>40 mL (2 multidose vials) (53.3 MME/day)</td>
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<tr>
<td>Methadone 10 mg/mL Intensol soln</td>
<td>q8-12h</td>
<td>60 mL (80 MME/day)</td>
<td>180 mL (80 MME/day)</td>
<td>90 mL (120 MME/day)</td>
</tr>
<tr>
<td>Methadone 5 mg/5 mL Oral soln</td>
<td>q8-12h</td>
<td>450 mL (60 MME/day)</td>
<td>1350 mL (60 MME/day)</td>
<td>600 mL (80 MME/day)</td>
</tr>
<tr>
<td>Methadone 10 mg/5 mL Oral soln</td>
<td>q8-12h</td>
<td>300 mL (80 MME/day)</td>
<td>900 mL (80 MME/day)</td>
<td>450 mL (120 MME/day)</td>
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<tr>
<td>MorphaBond ER 15 mg</td>
<td>q8-12h</td>
<td>90 tabs (45 MME/day)</td>
<td>270 tabs (45 MME/day)</td>
<td>120 tabs (60 MME/day)</td>
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<tr>
<td>MorphaBond ER 30 mg</td>
<td>q8-12h</td>
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<td>270 tabs (90 MME/day)</td>
<td>120 tabs (120 MME/day)</td>
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<tr>
<td>MorphaBond ER 60 mg</td>
<td>q8-12h</td>
<td>0*** (80 MME/day)</td>
<td>300 mL (80 MME/day)</td>
<td>1800 mL (80 MME/day)</td>
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<td>MorphaBond ER 100 mg</td>
<td>q8-12h</td>
<td>0*** (80 MME/day)</td>
<td>3000 mL (80 MME/day)</td>
<td>18000 mL (80 MME/day)</td>
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<td>MS Contin 15 mg</td>
<td>q8-12h</td>
<td>90 tabs (45 MME/day)</td>
<td>270 tabs (45 MME/day)</td>
<td>120 tabs (60 MME/day)</td>
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<td>MS Contin 30 mg</td>
<td>q8-12h</td>
<td>90 tabs (90 MME/day)</td>
<td>270 tabs (90 MME/day)</td>
<td>120 tabs (120 MME/day)</td>
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<tr>
<td>MS Contin 60 mg</td>
<td>q8-12h</td>
<td>0*** (180 MME/day)</td>
<td>90 tabs (180 MME/day)</td>
<td>270 tabs (180 MME/day)</td>
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<td>MS Contin 100 mg</td>
<td>q8-12h</td>
<td>0*** (180 MME/day)</td>
<td>60 tabs (200 MME/day)</td>
<td>180 tabs (200 MME/day)</td>
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<td>MS Contin 200 mg</td>
<td>q8-12h</td>
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<td>Nucynta ER 50 mg</td>
<td>q12h, MAX 500 mg/day</td>
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<td>Nucynta ER 100 mg</td>
<td>q12h, MAX 500 mg/day</td>
<td>60 tabs (80 MME/day)</td>
<td>180 tabs (80 MME/day)</td>
<td>90 tabs (120 MME/day)</td>
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<td>Nucynta ER 150 mg</td>
<td>q12h, MAX 500 mg/day</td>
<td>0*** (120 MME/day)</td>
<td>90 tabs (180 MME/day)</td>
<td>270 tabs (180 MME/day)</td>
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<tr>
<td>Nucynta ER 200 mg</td>
<td>q12h, MAX 500 mg/day</td>
<td>0*** (160 MME/day)</td>
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<td>Nucynta ER 250 mg</td>
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<td>Opana ER 5 mg</td>
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<td>Opana ER 7.5 mg</td>
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<td>Troxyca ER 30 mg/3.6 mg</td>
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<td>90 caps (90 MME/day)</td>
<td>270 caps (270 MME/day)</td>
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<td>Troxyca ER 60 mg/7.2 mg</td>
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<td>60 caps</td>
<td>90 caps (90 MME/day)</td>
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<tr>
<td>Troxyca ER 80 mg/9.6 mg</td>
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<td>Vantrela ER 15 mg</td>
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<td>Vantrela ER 20 mg/20 mg</td>
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<td>Vantrela ER 30 mg/30 mg</td>
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<td>90 tabs (90 MME/day)</td>
<td>270 tabs (270 MME/day)</td>
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<tr>
<td>Vantrela ER 40 mg/40 mg</td>
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<td>90 tabs (90 MME/day)</td>
<td>270 tabs (270 MME/day)</td>
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<tr>
<td>Vantrela ER 50 mg/50 mg</td>
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<tr>
<td>Vantrela ER 60 mg/60 mg</td>
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<td>Vantrela ER 50 mg</td>
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<tr>
<td>Vantrela ER 60 mg</td>
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<td>Vantrela ER 90 mg</td>
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</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Opioids ER mg</th>
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<th>Quantity</th>
<th>MME</th>
<th>Quantity</th>
<th>MME</th>
<th>Quantity</th>
<th>MME</th>
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<td>Xtampza ER 27 mg</td>
<td>q12h, MAX 288 mg/day</td>
<td>60 caps (90 MME/day)</td>
<td>180 caps (90 MME/day)</td>
<td>90 caps (135 MME/day)</td>
<td>270 caps (135 MME/day)</td>
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<tr>
<td>Xtampza ER 36 mg</td>
<td>q12h, MAX 288 mg/day</td>
<td>0***</td>
<td>0***</td>
<td>90 caps (180 MME/day)</td>
<td>270 caps (180 MME/day)</td>
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<tr>
<td>Zohydro ER 10 mg</td>
<td>q12h</td>
<td>60 caps (20 MME/day)</td>
<td>180 caps (20 MME/day)</td>
<td>90 caps (30 MME/day)</td>
<td>270 caps (30 MME/day)</td>
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<tr>
<td>Zohydro ER 15 mg</td>
<td>q12h</td>
<td>60 caps (30 MME/day)</td>
<td>180 caps (30 MME/day)</td>
<td>90 caps (45 MME/day)</td>
<td>270 caps (45 MME/day)</td>
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<tr>
<td>Zohydro ER 20 mg</td>
<td>q12h</td>
<td>60 caps (40 MME/day)</td>
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<td>90 caps (60 MME/day)</td>
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<tr>
<td>Zohydro ER 30 mg</td>
<td>q12h</td>
<td>60 caps (60 MME/day)</td>
<td>180 caps (60 MME/day)</td>
<td>90 caps (90 MME/day)</td>
<td>270 caps (90 MME/day)</td>
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<td>Zohydro ER 40 mg</td>
<td>q12h</td>
<td>60 caps (80 MME/day)</td>
<td>180 caps (80 MME/day)</td>
<td>90 caps (120 MME/day)</td>
<td>270 caps (120 MME/day)</td>
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<td>Zohydro ER 50 mg</td>
<td>q12h</td>
<td>0***</td>
<td>0***</td>
<td>60 caps (100 MME/day)</td>
<td>180 caps (100 MME/day)</td>
<td></td>
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</tr>
</tbody>
</table>

*The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing. Limits are set up as quantity versus time edits.

**Unless minimum FDA-labeled strength/dose/frequency exceeds 200 MME/day.

***The initial limit is zero. All requests for this drug and strength will be considered through post limit prior authorization.
## DURATION LIMIT WITH QUANTITY LIMIT AND POST LIMIT PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>IMMEDIATE-RELEASE OPIOID ANALGESICS (BRAND AND GENERIC)*</th>
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</thead>
<tbody>
<tr>
<td>generic name, dosage form</td>
<td>(codeine sulfate oral solution, tablets)</td>
</tr>
<tr>
<td></td>
<td>(levorphanol tartrate tablets)</td>
</tr>
<tr>
<td></td>
<td>(morphine sulfate oral soln, oral soln concentrate, suppositories, tablets)</td>
</tr>
<tr>
<td></td>
<td>(oxymorphone hydrochloride tablets)</td>
</tr>
<tr>
<td></td>
<td>(tapentadol oral solution, tablets)</td>
</tr>
</tbody>
</table>

**Status:** CVS Caremark Criteria  
**Type:** Initial Step; Duration Limit; Initial Limit; Post Limit PA  
Ref # 2221-M

*Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

### FDA-APPROVED INDICATIONS

**Codeine Sulfate**

**Oral Solution**

Codeine sulfate oral solution is an opioid analgesic indicated for the management of mild to moderately severe pain where the use of an opioid analgesic is appropriate.

**Tablets**

Codeine sulfate tablets are indicated for the management of mild to moderate pain, where treatment with an opioid is appropriate and for which alternative treatments are inadequate.

**Limitations of Use**
Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve codeine sulfate tablets for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or opioid combination products):

- Have not been tolerated or are not expected to be tolerated,
- Have not provided adequate analgesia or are not expected to provide adequate analgesia.

**Hydromorphone Hydrochloride**

*Oral Solution, Tablets*

Hydromorphone hydrochloride oral solution and hydromorphone hydrochloride tablets are indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

**Limitations of Use**

Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve hydromorphone hydrochloride oral solution and hydromorphone hydrochloride tablets for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or opioid combination products):

- Have not been tolerated or are not expected to be tolerated,
- Have not provided adequate analgesia or are not expected to provide adequate analgesia.

**Suppositories**

Hydromorphone hydrochloride is indicated for the relief of moderate to severe pain such as that due to: Surgery, Trauma (soft tissue and bone), Burns, Cancer, Biliary Colic, Myocardial Infarction, Renal Colic.

**Levorphanol Tartrate**

Levorphanol Tartrate tablets are indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

**Limitations of Use**

Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve levorphanol tartrate tablets for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or opioid combination products):

- Have not been tolerated or are not expected to be tolerated,
- Have not provided adequate analgesia or are not expected to provide adequate analgesia.

**Meperidine Hydrochloride**

*Oral Solution, Tablets*

Meperidine hydrochloride oral solution and tablets are indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

**Limitations of Use**

Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve meperidine hydrochloride oral solution and tablets for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or opioid combination products):

- Have not been tolerated or are not expected to be tolerated,
- Have not provided adequate analgesia or are not expected to provide adequate analgesia.

Meperidine hydrochloride oral solution and tablets should not be used for treatment of chronic pain. Prolonged meperidine use may increase the risk of toxicity (e.g., seizures) from the accumulation of the meperidine metabolite, normeperidine.

**Morphine Sulfate**

*Oral Solution*

Morphine sulfate oral solution 10 mg per 5 mL and 20 mg per 5 mL are formulations of morphine, an opioid agonist, indicated for the relief of moderate to severe acute and chronic pain where use of an opioid analgesic is appropriate. Morphine sulfate oral solution 100 mg per 5 mL (20 mg/mL) is an opioid analgesic indicated for the relief of moderate to severe acute and chronic pain in opioid-tolerant patients.

**Suppositories**

Morphine suppositories are indicated for the relief of severe chronic pain and severe acute pain.

**Tablets**

Opioids IR - 7-Day Acute Pain Duration Limit with MME Limit and Post Limit 2221-M 01-2019 (2) ©2019 CVS Caremark. All rights reserved.
Morphine sulfate tablets and suppositories are indicated for the management of acute and chronic pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

**Limitations of Use**

Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve morphine sulfate tablets for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or opioid combination products):
- Have not been tolerated or are not expected to be tolerated,
- Have not provided adequate analgesia or are not expected to provide adequate analgesia.

**Nucynta (tapentadol)**

**Oral Solution and Tablets**

Nucynta (tapentadol) oral solution and tablets are indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate in adults.

**Limitations of Use**

Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve Nucynta (tapentadol) oral solution and tablets for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or opioid combination products):
- Have not been tolerated or are not expected to be tolerated,
- Have not provided adequate analgesia or are not expected to provide adequate analgesia.

**Oxaydo (oxycodone hydrochloride)**

Oxaydo (oxycodone hydrochloride) is indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

**Limitations of Use**

Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve Oxaydo (oxycodone hydrochloride) for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or opioid combination products):
- Have not been tolerated or are not expected to be tolerated,
- Have not provided adequate analgesia or are not expected to provide adequate analgesia.

**Oxycodone Hydrochloride**

Capsules, Oral Concentrate, Oral Solution and Tablets

Oxycodone hydrochloride capsules, oral concentrate, oral solution and tablets are indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

**Limitations of Use**

Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve oxycodone hydrochloride capsules, oral concentrate, oral solution, and tablets for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or opioid combination products):
- Have not been tolerated or are not expected to be tolerated,
- Have not provided adequate analgesia or are not expected to provide adequate analgesia.

**Oxymorphone Hydrochloride**

Oxymorphone hydrochloride tablets are indicated for the management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

**Limitations of Use**

Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve oxymorphone hydrochloride tablets for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or opioid combination products):
- Have not been tolerated or are not expected to be tolerated,
- Have not provided adequate analgesia or are not expected to provide adequate analgesia.

**Pentazocine/Naloxone**

Pentazocine and naloxone tablets are indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.
Limitations of Use
Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve pentazocine and naloxone tablets for use in patients for whom alternative treatment options (e.g., non-opioid analgesics):

- Have not been tolerated or are not expected to be tolerated,
- Have not provided adequate analgesia or are not expected to provide adequate analgesia.

**RoxyBond (oxycodone hydrochloride)**
RoxyBond (oxycodone hydrochloride) is indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

**Limitations of Use**
Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve RoxyBond (oxycodone hydrochloride) for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or opioid combination products):

- Have not been tolerated or are not expected to be tolerated,
- Have not provided adequate analgesia or are not expected to provide adequate analgesia.

**Ultram (tramadol)**
Ultram (tramadol) is indicated for the management of pain in adults that is severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

**Limitations of Use**
Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve Ultram (tramadol) for use in patients for whom alternative treatment options (e.g., non-opioid analgesics):

- Have not been tolerated or are not expected to be tolerated,
- Have not provided adequate analgesia or are not expected to provide adequate analgesia.

**COVERAGE CRITERIA**
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for pain associated with cancer, sickle cell disease, a terminal condition, or pain being managed through hospice or palliative care

OR

- The patient can safely take the requested dose based on their history of opioid use. [Note: The lowest effective dosage should be prescribed for opioid naïve patients.]

AND

- The patient has been evaluated and the patient will be monitored regularly for the development of opioid use disorder

AND

- The requested drug is being prescribed for moderate to severe CHRONIC pain where use of an opioid analgesic is appropriate. [Note: Chronic pain is generally defined as pain that typically lasts greater than 3 months.]

AND

- The patient’s pain will be reassessed in the first month after the initial prescription or any dose increase AND every 3 months thereafter to ensure that clinically meaningful improvement in pain and function outweigh risks to patient safety

OR

- The patient requires extended treatment beyond 7 days for moderate to severe ACUTE pain where use of an opioid analgesic is appropriate

Quantity Limits may apply.
RATIONALE
The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Codeine sulfate is indicated for the management of mild to moderate pain, where treatment with an opioid is appropriate and for which alternative treatments are inadequate. Hydromorphone hydrochloride, levorphanol tartrate, meperidine, oxycodone hydrochloride, pentazocine/naloxone, tapentadol, and tramadol are indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. Morphine sulfate is indicated for the management of acute and chronic pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. Oxymorphone hydrochloride is indicated for the relief of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve immediate-release opioids for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or opioid combination products) 1) have not been tolerated or are not expected to be tolerated, or 2) have not provided adequate analgesia or are not expected to provide adequate analgesia.1-22

If the patient has filled a prescription for at least a 1-day supply of a drug indicating the patient is being treated for cancer or sickle cell disease (SCD) within the past 365 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

If a claim is submitted with an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

If the patient has an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in their member health profile in the past 365 days, then the requested drug will be paid under that prescription benefit.

If a claim is submitted using a hospice patient residence code under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

For patients with no prescription claims of a cancer drug or a sickle cell disease drug in the past 365 days, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care submitted with their prescription claim, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in the member health profile in the past 365 days, or no hospice patient residence code submitted with their prescription claim:
If the patient has filled a prescription for at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history in the past 90 days under a prescription benefit administered by CVS Caremark, then the initial quantity limit criteria will apply (see Column A and Column B in the Opioid Analgesics IR Quantity Limits Chart below).
If the patient does not have at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history in the past 90 days (i.e., this is the patient’s first fill of an opioid) and the incoming prescription drug is being filled for more than a 7-day supply, then the claim will reject with a message indicating that the patient can receive a 7-day supply or submit a prior authorization (PA) for additional quantities. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit. If the incoming prescription drug is being filled for less than a 7-day supply, then the initial quantity limit criteria will apply (see Column A and Column B in the Opioid Analgesics IR Quantity Limits Chart below).

The Centers for Disease Control and Prevention (CDC) Guideline for Prescribing Opioids for Chronic Pain provides recommendations for primary care clinicians who are prescribing opioids for chronic pain outside of active cancer treatment, sickle cell disease, palliative care, and end-of-life care. The National Comprehensive Cancer Network (NCCN) guidelines for Adult Cancer Pain recommend for continuous pain, it is appropriate to give pain medication on a regular schedule with supplemental doses for breakthrough pain. Add an extended-release or long-acting formulation to provide background analgesia for control of chronic persistent pain controlled on stable doses of short-acting opioids.
When possible, use the same opioid for short-acting and extended-release forms. Allow rescue doses of short-acting opioids up to every 1 hour as needed. The NCCN Palliative Care pain management recommendation is to treat according to NCCN guidelines for adult cancer pain. For patients with no prescription claims of a cancer drug in the past 365 days, no ICD 10 diagnosis code indicating cancer or palliative care submitted with their prescription claim, no ICD 10 diagnosis code indicating cancer or palliative care in the member health profile in the past 365 days, or no hospice patient residence code submitted with their prescription claim who are identified through the prior authorization criteria as having cancer, a terminal condition, or pain being managed through hospice or palliative care, acute pain duration limits and post limit quantities will not apply.

According to the National Heart, Lung, and Blood Institute’s (NHLBI) guidelines for Sickle Cell Disease (SCD), pain is the most common symptom of SCD. Pain can be acute, chronic, or an acute episode superimposed on chronic pain. Recurrent acute pain crises (also known as vaso-occlusive crises) are the most common manifestation of SCD. Chronic pain is also one of the most common chronic complications of SCD. Pain management must be guided by patient report of severity. No biomarkers or imaging studies can validate pain or assess its severity. Medications used to treat SCD-related pain should be tailored to the individual. For pain that is not relieved by nonsteroidal anti-inflammatory drugs (NSAIDs) or other measures, either short-acting or long-acting opioids may be used to manage pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed. Coverage is provided for up to 7 days initially to provide an amount sufficient for the treatment of acute pain.

Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, then clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.

Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should consider history of overdose, history of substance use disorder, higher opioid dosages [≥50 morphine milligram equivalents per day (MME/day)], or concurrent benzodiazepine use. The CDC Guideline for Prescribing Opioids for Chronic Pain recommends that when opioids are started, clinicians should prescribe the lowest effective dose of immediate-release opioids and should not prescribe a greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed. Coverage is provided for up to 7 days initially to provide an amount sufficient for the treatment of acute pain.

The American Pain Society Opioid Treatment Guidelines state that a reasonable definition for high dose opioid therapy is >200 mg daily of oral morphine (or equivalent). The immediate-release opioid drug post limit quantities are set to encompass the usual dosage and frequency range recommendations in labeling without exceeding a monthly quantity that corresponds to 90 MME/day. If the patient is requesting more than the initial quantity limit, then the system will reject with a message indicating that a prior authorization is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

Opioids IR - 7-Day Acute Pain Duration Limit with MME Limit and Post Limit 2221-M 01-2019 (2)
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Although meperidine is commonly used for acute pain relief, use of this drug as first-line opiate therapy is discouraged because of central excitatory toxicity of the metabolite (normeperidine). Because of extensive first-pass metabolism in the liver of normeperidine, the risk of excitatory toxicity is increased with oral administration of meperidine. Therefore, oral therapy is discouraged. Use of meperidine for chronic pain is discouraged because of its short duration of effect and risk of accumulation. Meperidine should be limited to short-term (i.e., a few days) because of the risk of accumulation of the toxic normeperidine metabolite with repeated or large doses.\(^\text{21}\) The initial quantity limit for meperidine will be set at a quantity that corresponds to a 72 hour supply (allows for weekend coverage, if necessary). The post limit quantity will be set at a quantity that corresponds to a 96 hour supply, allowing one additional day of therapy beyond the initial quantity limit.

The limit for codeine is set reflective of its questionable role in chronic or moderate to severe pain management as compared to other opioid medications. When prescribing codeine, healthcare providers should choose the lowest effective dose for the shortest period of time. The initial quantity limit for codeine will be set at a quantity that corresponds to a one week supply. The post limit quantity will be set at a quantity that corresponds to a two-week supply.

Pentazocine is not commonly used in clinical practice due to the occurrence of dysphoric reactions and its relatively short duration of action.\(^\text{27}\) According to the NCCN Guidelines for Adult Cancer Pain, mixed agonist-antagonist drugs (including pentazocine) have limited usefulness and are not recommended for the treatment of cancer pain.\(^\text{24}\) The one month and three months limit for pentazocine/naloxone are set as the same based on these significant safety concerns.

**PROGRAM DESCRIPTION**
Neither acute pain duration limits nor quantity limits apply if the patient has a drug in claims history in the past year that indicates the patient is being treated for cancer or sickle cell disease. In addition, neither acute pain duration limits nor quantity limits will apply if a prescription claim is submitted with an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care, if the patient has an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in their member health profile in the past 365 days, or if a prescription claim is submitted using a hospice patient residence code.

**Acute Pain Duration Limit**
If a patient has filled a prescription for at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history in the past 90 days, then the immediate-release opioid will adjudicate for up to the initial quantity limit.

If the patient does not have at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history in the past 90 days (i.e., this is the patient's first fill of an opioid), then coverage is provided for up to a 7-day supply of the immediate-release opioid. Prior authorization review is required to determine coverage for a quantity necessary for treatment beyond 7 days. For patients with no prescription claims of a cancer drug or a sickle cell disease drug in the past 365 days, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care submitted with their prescription claim, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in the member health profile in the past 365 days, or no hospice patient residence code submitted with their prescription claim who are identified through the prior authorization criteria as having cancer, sickle cell disease, a terminal condition, or pain being managed through hospice or palliative care, acute pain duration limits will not apply.

**Quantity Limit/Post Limit**
Plans implementing morphine milligram equivalent (MME)-based quantity limits on immediate-release opioids are providing coverage for an initial amount of a monthly quantity that corresponds to 90 MME or less per day. Coverage is provided for up to the initial quantity limit per Column A and Column B in the Opioid Analgesics IR Quantity Limits Chart below.
Prior authorization review is required to determine coverage for additional quantities above the initial limit.

Post limit quantities are set not to exceed a monthly quantity that corresponds to 200 MME/day. For patients with no prescription claims of a cancer drug or a sickle cell disease drug in the past 365 days, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care submitted with their prescription claim, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in the member health profile in the past 365 days, or no hospice patient residence code submitted with their prescription claim who are identified through the prior authorization criteria as having cancer, sickle cell disease, a terminal condition, or pain being managed through hospice or palliative care, post limit quantities will not apply.

*Acute Pain Duration Limit logic will apply first, followed by initial quantity limit logic.

REFERENCES

8. Morphine Sulfate 10 mg/5 mL, 20 mg/5 mL, 100 mg/5 mL (20 mg/mL) oral solution [package insert]. Bryan, OH: Nostrum Laboratories, Inc.; December 2018.
16. Oxycodone Hydrochloride 5 mg/5 mL, 100 mg/5 mL (20 mg/mL) oral solution [package insert]. Newtown, PA: KVK-TECH, Inc.; December 2018.
INITIAL STEP THERAPY

If the patient has filled a prescription for at least a 1-day supply of a drug indicating the patient is being treated for cancer or sickle cell disease within the past 365 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

If a claim is submitted with an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

If the patient has an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in their member health profile in the past 365 days, then the requested drug will be paid under that prescription benefit.

If a claim is submitted using a hospice patient residence code under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

For patients with no prescription claims of a cancer drug or a sickle cell disease drug in the past 365 days, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care submitted with their prescription claim, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in the member health profile in the past 365 days, or no hospice patient residence code submitted with their prescription claim:

If the patient has filled a prescription for at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history in the past 90 days under a prescription benefit administered by CVS Caremark, then the initial quantity limit criteria will apply (see Column A and Column B in the Opioid Analgesics IR Quantity Limits Chart below).

If the patient does not have at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history in the past 90 days (i.e., this is the patient’s first fill of an opioid) and the incoming prescription drug is being filled for more than a 7-day supply, then the claim will reject with a message indicating that the patient can receive a 7-day supply or submit a prior authorization (PA) for additional quantities. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit. If the incoming prescription drug is being filled for less than a 7-day supply, then the initial quantity limit criteria will apply (see Column A and Column B in the Opioid Analgesics IR Quantity Limits Chart below).
LIMIT CRITERIA:
Neither acute pain duration limits nor quantity limits apply if the patient has a drug in claims history in the past year that indicates the patient is being treated for cancer or sickle cell disease. In addition, neither acute pain duration limits nor quantity limits will apply if a prescription claim is submitted with an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care, if the patient has an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in their member health profile in the past 365 days, or if a prescription claim is submitted using a hospice patient residence code.

ACUTE PAIN DURATION LIMIT:
The acute pain duration limit portion of this program applies to patients identified with potential first fills of immediate-release opioid prescriptions for the treatment of non-cancer and non-sickle cell related pain. A first fill is defined as at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history during the past 90 days.

If the patient does not have at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history in the past 90 days (i.e., this is the patient’s first fill of an opioid) and the incoming prescription drug is being filled for more than a 7-day supply, then the claim will reject with a message indicating that the patient can receive a 7-day supply or submit a prior authorization (PA) for additional quantities. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit. If the incoming prescription drug is being filled for less than a 7-day supply, then the initial quantity limit criteria will apply (see Column A and Column B in the Opioid Analgesics IR Quantity Limits Chart below).

INITIAL QUANTITY LIMIT:
Morphine milligram equivalent (MME) quantity limits for immediate-release opioids provide coverage for an initial amount of a monthly quantity that corresponds to 90 MME or less per day. Coverage is provided for up to the initial quantity limit per Column A and Column B in the Opioid Analgesics IR Quantity Limits Chart below. Prior authorization review is required to determine coverage for additional quantities above the initial limit.

*Acute Pain Duration Limit logic will apply first, followed by initial quantity limit logic.

CRITERIA FOR APPROVAL

<table>
<thead>
<tr>
<th></th>
<th>Question</th>
<th>Yes</th>
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</tr>
</thead>
</table>
| 1 | Is the requested drug being prescribed for pain associated with cancer, sickle cell disease, a terminal condition, or pain being managed through hospice or palliative care?  
   [If yes, then no further questions.]                                      |     |    |
| 2 | Can the patient safely take the requested dose based on their history of opioid use?  
   [Note: The lowest effective dosage should be prescribed for opioid naïve patients.] |     |    |
| 3 | Has the patient been evaluated and will the patient be monitored regularly for the development of opioid use disorder? |     |    |
| 4 | Is the requested drug being prescribed for moderate to severe CHRONIC pain where use of an opioid analgesic is appropriate?  
   [Note: Chronic pain is generally defined as pain that typically lasts greater than 3 months.]  
   [If no, then skip to question 6.]                                           |     |    |
5. Will the patient’s pain be reassessed in the first month after the initial prescription or any dose increase AND every 3 months thereafter to ensure that clinically meaningful improvement in pain and function outweigh risks to patient safety?  
[If yes, then skip to question 7.]

6. Does the patient require extended treatment beyond 7 days for moderate to severe ACUTE pain where use of an opioid analgesic is appropriate?  
[If yes, then skip to question 8.]  
[If no, then no further questions.]

7. Which drug is being requested (applies to brand or generic)?  
[Note: Please check the drug being requested (applies to brand or generic).]

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>codeine oral solution or tablets</td>
<td></td>
<td></td>
</tr>
<tr>
<td>hydromorphone oral solution, suppositories, or tablets</td>
<td></td>
<td></td>
</tr>
<tr>
<td>levorphanol tablets (if checked, go to 10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>meperidine oral solution or tablets (if checked, go to 20)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>morphine sulfate oral concentrate or oral solution (if checked, go to 13)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>morphine sulfate suppositories (if checked, go to question 14)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>morphine sulfate tablets (if checked, go to question 15)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>oxycodone, Oxyado, or RoxyBond capsules or tablets (if checked, go to question 16)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>oxycodone oral concentrate or oral solution (if checked, go to 17)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>oxymorphone tablets (if checked, go to question 18)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>pentazocine/naloxone tablets (if checked, go to 19)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>tapentadol oral solution or tablets (Nucynta) (if checked, go to 20)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>tramadol tablets (if checked, go to 21)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

8. Which drug is being requested (applies to brand or generic)?  
[Note: Please check the drug being requested (applies to brand or generic).]

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>codeine oral solution or tablets</td>
<td></td>
<td></td>
</tr>
<tr>
<td>hydromorphone oral solution, suppositories, or tablets</td>
<td></td>
<td></td>
</tr>
<tr>
<td>levorphanol tablets (if checked, go to 24)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>meperidine oral solution or tablets (if checked, go to 25)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>morphine sulfate oral concentrate or oral solution (if checked, go to 26)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>morphine sulfate suppositories (if checked, go to question 27)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>morphine sulfate tablets (if checked, go to question 28)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>oxycodone, Oxyado, or RoxyBond capsules or tablets (if checked, go to question 29)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>oxycodone oral concentrate or oral solution (if checked, go to 30)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>oxymorphone tablets (if checked, go to question 31)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>pentazocine/naloxone tablets (if checked, go to 32)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>tapentadol oral solution or tablets (Nucynta) (if checked, go to 33)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>tramadol tablets (if checked, go to 34)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

9. Does the patient require use of MORE than the plan allowance of 840 mL (quantity sufficient for a 14-day supply) in a one month period of codeine sulfate oral solution OR MORE than the plan allowance of 84 tablets (quantity sufficient for a 14-day supply) in a one month period of codeine sulfate tablets?  
[No further questions.]  

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Does the patient require use of MORE than the plan allowance PER MONTH of any of the following: A) 1500 mL of hydromorphone oral solution, B) 180 suppositories of hydromorphone suppositories, C) 270 tablets of hydromorphone 2 mg tablets, D) 225 tablets of hydromorphone 4 mg tablets, E) 90 tablets of hydromorphone 8 mg tablets? [No further questions.]</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>10</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>[RPh Note: If yes, then deny and enter a partial approval for ONE of the following: A) 1500 mL/month of hydromorphone oral solution, B) 180 suppositories/month of hydromorphone suppositories, C) 270 tablets/month of hydromorphone 2 mg tablets, D) 225 tablets/month of hydromorphone 4 mg tablets, E) 90 tablets/month of hydromorphone 8 mg tablets. ]</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td>11</td>
<td>Does the patient require use of MORE than the plan allowance PER MONTH of 180 levorphanol tablets? [No further questions.]</td>
</tr>
<tr>
<td></td>
<td>[RPh Note: If yes, then deny and enter a partial approval for 180 levorphanol tablets/month. ]</td>
</tr>
<tr>
<td>12</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Does the patient require use of MORE than the plan allowance of 120 mL (quantity sufficient for a 4-day supply) in a one month period of meperidine oral solution OR MORE than the plan allowance of 24 tablets/month (quantity sufficient for a 4-day supply) of meperidine tablets in a one month period? [No further questions.]</td>
</tr>
<tr>
<td></td>
<td>[RPh Note: If yes, then deny and enter a partial approval for 120 mL/month of meperidine oral solution OR 24 tablets/month of meperidine tablets. ]</td>
</tr>
<tr>
<td>13</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Does the patient require use of MORE than the plan allowance PER MONTH of 270 mL of morphine sulfate 20 mg/mL (100 mg/5 mL) oral concentrate solution OR MORE than the plan allowance PER MONTH of 1350 mL of morphine sulfate 10 mg/5 mL or 20 mg/5 mL oral solution? [No further questions.]</td>
</tr>
<tr>
<td></td>
<td>[RPh Note: If yes, then deny and enter a partial approval for 270 mL/month of morphine sulfate 20 mg/mL (100 mg/5 mL) oral concentrate solution OR 1350 mL/month of morphine sulfate 10 mg/5 mL or 20 mg/5 mL oral solution. ]</td>
</tr>
<tr>
<td>14</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Does the patient require use of MORE than the plan allowance PER MONTH of 270 suppositories of morphine sulfate suppository 5 mg, 10 mg, 20 mg OR MORE than the plan allowance PER MONTH of 180 suppositories of morphine sulfate suppository 30 mg? [No further questions.]</td>
</tr>
<tr>
<td></td>
<td>[RPh Note: If yes, then deny and enter a partial approval for 270 suppositories/month of morphine sulfate suppository 5 mg, 10 mg, 20 mg OR 180 suppositories/month of morphine sulfate suppository 30 mg. ]</td>
</tr>
<tr>
<td>Question</td>
<td>Yes</td>
</tr>
<tr>
<td>-------------------------------------------------------------------------</td>
<td>-----</td>
</tr>
<tr>
<td><strong>15.</strong> Does the patient require use of MORE than the plan allowance PER MONTH of 270 tablets of morphine sulfate 15 mg tablets OR MORE than the plan allowance PER MONTH of 180 tablets of morphine sulfate 30 mg tablets? [No further questions.]</td>
<td></td>
</tr>
<tr>
<td>[RPh Note: If yes, then deny and enter a partial approval for 270 tablets/month of morphine sulfate 15 mg tablets OR 180 tablets/month of morphine sulfate 30 mg tablets.]</td>
<td></td>
</tr>
<tr>
<td><strong>16.</strong> Does the patient require use of MORE than the plan allowance PER MONTH of any of the following: A) 270 capsules or tablets of oxycodone 5 mg, 10 mg, Oxaydo 5 mg or 7.5 mg, or RoxyBond 5 mg, B) 180 tablets of oxycodone 15 mg, 20 mg, or RoxyBond 15 mg C) 120 tablets of oxycodone 30 mg or RoxyBond 30 mg? [No further questions.]</td>
<td></td>
</tr>
<tr>
<td>[RPh Note: If yes, then deny and enter a partial approval for ONE of the following: A) 270 capsules or tablets/month of oxycodone 5 mg, 10 mg, Oxaydo 5 mg or 7.5 mg, or RoxyBond 5 mg, B) 180 tablets/month of oxycodone 15 mg, 20 mg, or RoxyBond 15 mg C) 120 tablets/month of oxycodone 30 mg or RoxyBond 30 mg.]</td>
<td></td>
</tr>
<tr>
<td><strong>17.</strong> Does the patient require use of MORE than the plan allowance PER MONTH of 180 mL of oxycodone 100 mg/5 mL (20 mg/mL) oral concentrate OR MORE than the plan allowance PER MONTH of 2700 mL of oxycodone 5 mg/5 mL oral solution? [No further questions.]</td>
<td></td>
</tr>
<tr>
<td>[RPh Note: If yes, then deny and enter a partial approval for 180 mL/month of oxycodone 100 mg/5 mL (20 mg/mL) oral concentrate OR 2700 mL/month of oxycodone 5 mg/5 mL oral solution.]</td>
<td></td>
</tr>
<tr>
<td><strong>18.</strong> Does the patient require use of MORE than the plan allowance PER MONTH of 360 tablets of oxymorphone 5 mg OR MORE than the plan allowance PER MONTH of 180 tablets of oxymorphone 10 mg? [No further questions.]</td>
<td></td>
</tr>
<tr>
<td>[RPh Note: If yes, then deny and enter a partial approval for 360 tablets/month of oxymorphone 5 mg OR 180 tablets/month of oxymorphone 10 mg.]</td>
<td></td>
</tr>
<tr>
<td><strong>19.</strong> Does the patient require use of MORE than the plan allowance PER MONTH of 300 pentazocine/naloxone tablets? [No further questions.]</td>
<td></td>
</tr>
<tr>
<td>[RPh Note: If yes, then deny and enter a partial approval for 300 pentazocine/naloxone tablets/month.]</td>
<td></td>
</tr>
<tr>
<td><strong>20.</strong> Does the patient require use of MORE than the plan allowance PER MONTH of any of the following: A) 240 tablets of Nucynta (tapentadol) 50 mg tablets, B) 180 tablets of Nucynta (tapentadol) 75 mg tablets, C) 120 tablets of Nucynta (tapentadol) 100 mg tablets, D) 700 mL of Nucynta (tapentadol) oral solution? [No further questions.]</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
[RPh Note: If yes, then deny and enter a partial approval for ONE of the following: A) 240 tablets/month of Nucynta (tapentadol) 50 mg tablets, B) 180 tablets/month of Nucynta (tapentadol) 75 mg tablets, C) 120 tablets/month of Nucynta (tapentadol) 100 mg tablets, D) 700 mL/month of Nucynta (tapentadol) oral solution.]

21 Does the patient require use of MORE than the plan allowance PER MONTH of 240 tablets of tramadol? Yes No
[No further questions.]

[RPh Note: If yes, then deny and enter a partial approval for 240 tablets/month of tramadol.]

22 Does the patient require use of MORE than the plan allowance of 840 mL (quantity sufficient for a 14-day supply) in a one month period of codeine sulfate oral solution OR MORE than the plan allowance of 84 tablets (quantity sufficient for a 14-day supply) in a one month period of codeine sulfate tablets? Yes No
[No further questions.]

[RPh Note: If yes, then deny and enter a partial approval for 840 mL/month of codeine sulfate oral solution OR 84 tablets/month of codeine sulfate tablets.]

23 Does the patient require use of MORE than the plan allowance PER MONTH of any of the following: A) 1500 mL of hydromorphone oral solution, B) 180 suppositories of hydromorphone suppositories, C) 270 tablets of hydromorphone 2 mg tablets, D) 225 tablets of hydromorphone 4 mg tablets, E) 90 tablets of hydromorphone 8 mg tablets? Yes No
[No further questions.]

[RPh Note: If yes, then deny and enter a partial approval for ONE of the following: A) 1500 mL/month of hydromorphone oral solution, B) 180 suppositories/month of hydromorphone suppositories, C) 270 tablets/month of hydromorphone 2 mg tablets, D) 225 tablets/month of hydromorphone 4 mg tablets, E) 90 tablets/month of hydromorphone 8 mg tablets.]

24 Does the patient require use of MORE than the plan allowance PER MONTH of 180 levorphanol tablets? Yes No
[No further questions.]

[RPh Note: If yes, then deny and enter a partial approval for 180 levorphanol tablets/month.]

25 Does the patient require use of MORE than the plan allowance of 120 mL (quantity sufficient for a 4-day supply) in a one month period of meperidine oral solution OR MORE than the plan allowance of 24 tablets/month (quantity sufficient for a 4-day supply) of meperidine tablets in a one month period? Yes No
[No further questions.]

[RPh Note: If yes, then deny and enter a partial approval for 120 mL/month of meperidine oral solution OR 24 tablets/month of meperidine tablets.]
26. Does the patient require use of MORE than the plan allowance PER MONTH of 270 mL of morphine sulfate 20 mg/mL (100 mg/5 mL) oral concentrate solution OR MORE than the plan allowance PER MONTH of 1350 mL of morphine sulfate 10 mg/5 mL or 20 mg/5 mL oral solution? [No further questions.]

[RPh Note: If yes, then deny and enter a partial approval for 270 mL/month of morphine sulfate 20 mg/mL (100 mg/5 mL) oral concentrate solution OR 1350 mL/month of morphine sulfate 10 mg/5 mL or 20 mg/5 mL oral solution.]

27. Does the patient require use of MORE than the plan allowance PER MONTH of 270 suppositories of morphine sulfate suppository 5 mg, 10 mg, 20 mg OR MORE than the plan allowance PER MONTH of 180 suppositories of morphine sulfate suppository 30 mg? [No further questions.]

[RPh Note: If yes, then deny and enter a partial approval for 270 suppositories/month of morphine sulfate suppository 5 mg, 10 mg, 20 mg OR 180 suppositories/month of morphine sulfate suppository 30 mg.]

28. Does the patient require use of MORE than the plan allowance PER MONTH of 270 tablets of morphine sulfate 15 mg tablets OR MORE than the plan allowance PER MONTH of 180 tablets of morphine sulfate 30 mg tablets? [No further questions.]

[RPh Note: If yes, then deny and enter a partial approval for 270 tablets/month of morphine sulfate 15 mg tablets OR 180 tablets/month of morphine sulfate 30 mg tablets.]

29. Does the patient require use of MORE than the plan allowance PER MONTH of any of the following: A) 270 capsules or tablets of oxycodone 5 mg, 10 mg, Oxydo 5 mg or 7.5 mg, or RoxyBond 5 mg, B) 180 tablets of oxycodone 15 mg, 20 mg, or RoxyBond 15 mg C) 120 tablets of oxycodone 30 mg or RoxyBond 30 mg? [No further questions.]

[RPh Note: If yes, then deny and enter a partial approval for ONE of the following: A) 270 capsules or tablets/month of oxycodone 5 mg, 10 mg, Oxydo 5 mg or 7.5 mg, or RoxyBond 5 mg, B) 180 tablets/month of oxycodone 15 mg, 20 mg, or RoxyBond 15 mg C) 120 tablets/month of oxycodone 30 mg or RoxyBond 30 mg.]

30. Does the patient require use of MORE than the plan allowance PER MONTH of 180 mL of oxycodone 100 mg/5 mL (20 mg/mL) oral concentrate OR MORE than the plan allowance PER MONTH of 2700 mL of oxycodone 5 mg/5 mL oral solution? [No further questions.]

[RPh Note: If yes, then deny and enter a partial approval for 180 mL/month of oxycodone 100 mg/5 mL (20 mg/mL) oral concentrate OR 2700 mL/month of oxycodone 5 mg/5 mL oral solution.]
31. Does the patient require use of MORE than the plan allowance PER MONTH of 360 tablets of oxymorphone 5 mg OR MORE than the plan allowance PER MONTH of 180 tablets of oxymorphone 10 mg?

[No further questions.]

[RPh Note: If yes, then deny and enter a partial approval for 360 tablets/month of oxymorphone 5 mg OR 180 tablets/month of oxymorphone 10 mg.]

Yes  No

32. Does the patient require use of MORE than the plan allowance PER MONTH of 300 pentazocine/naloxone tablets?

[No further questions.]

[RPh Note: If yes, then deny and enter a partial approval for 300 pentazocine/naloxone tablets/month.]

Yes  No

33. Does the patient require use of MORE than the plan allowance PER MONTH of any of the following: A) 240 tablets of Nucynta (tapentadol) 50 mg tablets, B) 180 tablets of Nucynta (tapentadol) 75 mg tablets, C) 120 tablets of Nucynta (tapentadol) 100 mg tablets, D) 700 mL of Nucynta (tapentadol) oral solution?

[No further questions.]

[RPh Note: If yes, then deny and enter a partial approval for ONE of the following: A) 240 tablets/month of Nucynta (tapentadol) 50 mg tablets, B) 180 tablets/month of Nucynta (tapentadol) 75 mg tablets, C) 120 tablets/month of Nucynta (tapentadol) 100 mg tablets, D) 700 mL/month of Nucynta (tapentadol) oral solution.]

Yes  No

34. Does the patient require use of MORE than the plan allowance PER MONTH of 240 tablets of tramadol?

[No further questions.]

[RPh Note: If yes, then deny and enter a partial approval for 240 tablets/month of tramadol.]

Yes  No

---

**Mapping Instructions**

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
<th>DENIAL REASONS – DO NOT USE FOR MEDICARE PART D</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Go to 2</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you can safely take the drug based on your history of opioid use. Your request has been denied based on the information we have.</td>
</tr>
</tbody>
</table>

- **Go to 2**

- Deny
<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>3. Go to 4</td>
<td>Deny</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you will be monitored regularly. Your request has been denied based on the information we have. [Short Description: Patient not monitored regularly for opioid use disorder.]</td>
</tr>
<tr>
<td>4. Go to 5</td>
<td>Go to 6</td>
<td></td>
</tr>
<tr>
<td>5. Go to 7</td>
<td>Deny</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: - Your pain will be checked by your doctor the first month after your initial prescription or after a dose increase and every 3 months after that - The benefits outweigh the risks of taking the medication Your request has been denied based on the information we have. [Short Description: Patient's pain is not being reassessed.]</td>
</tr>
<tr>
<td>6. Go to 8</td>
<td>Deny</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have one of these conditions: - Pain due to cancer, sickle cell disease, or a terminal condition - Pain being managed through hospice or palliative care - Moderate to severe chronic pain that requires treatment with an opioid - Moderate to severe acute pain that requires treatment with an opioid for more than seven days Your request has been denied based on the information we have. [Short Description: No approvable diagnosis.]</td>
</tr>
<tr>
<td>7.</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>8.</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>9. Deny</td>
<td>Approve, 12 months</td>
<td>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 840 mL of codeine sulfate oral solution in a one month period - 84 tablets of codeine sulfate tablets in a one month period You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity.]</td>
</tr>
</tbody>
</table>

RPh Note: For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.
<table>
<thead>
<tr>
<th></th>
<th>Deny</th>
<th>RPh Note: For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.</th>
<th>Approve, 12 months</th>
<th>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>Deny</td>
<td>See Opioid Analgesics IR Quantity Limits Chart (Column C for 1 month supply or Column D for a 3 month supply)</td>
<td>- 1500 mL/month of hydromorphone oral solution</td>
<td>- 180 suppositories/month hydromorphone suppositories</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- 270 tablets/month of hydromorphone 2 mg tablets</td>
<td>- 225 tablets/month of hydromorphone 4 mg tablets</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- 90 tablets/month of hydromorphone 8 mg tablets</td>
<td>You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>[Short Description: Over max quantity.]</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Deny</td>
<td>Approve, 12 months</td>
<td>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 180 tablets/month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.</td>
<td>[Short Description: Over max quantity.]</td>
</tr>
<tr>
<td>12</td>
<td>Deny</td>
<td>See Opioid Analgesics IR Quantity Limits Chart (Column C for 1 month supply or Column D for a 3 month supply)</td>
<td>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- 120 mL of meperidine oral solution in a one month period</td>
<td>- 24 tablets of meperidine tablets in a one month period</td>
<td>You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>[Short Description: Over max quantity.]</td>
<td>[Short Description: Over max quantity.]</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>Deny</td>
<td>Approve, 12 months</td>
<td>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>See Opioid Analgesics IR Quantity Limits Chart (Column C for 1 month supply or Column D for a 3 month supply)</td>
<td>- 270 mL/month of morphine sulfate 20 mg/mL (100 mg/5 mL) oral concentrate solution</td>
<td>- 1350 mL/month of morphine sulfate 10 mg/5 mL or 20 mg/5 mL oral solution</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.</td>
<td>[Short Description: Over max quantity.]</td>
</tr>
<tr>
<td>14</td>
<td>Deny</td>
<td>See Opioid Analgesics IR</td>
<td>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Approve, 12 months</td>
<td>- 270 suppositories/month of morphine sulfate suppository 5 mg, 10 mg, or 20 mg</td>
<td>- 180 suppositories/month of morphine sulfate suppository 30 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>[Short Description: Over max quantity.]</td>
<td></td>
</tr>
</tbody>
</table>

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| Remove all the other drugs from the verbiage. | Quantity Limits Chart (Column C for 1 month supply or Column D for a 3 month supply) | You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.  
[Short Description: Over max quantity.]

15. Deny  
RPh Note: For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage. | Approve, 12 months  
See Opioid Analgesics IR Quantity Limits Chart (Column C for 1 month supply or Column D for a 3 month supply) | You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:  
- 270 tablets/month of morphine sulfate 15 mg tablets  
- 180 tablets/month of morphine sulfate 30 mg tablets  
You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.  
[Short Description: Over max quantity.]

16. Deny  
RPh Note: For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage. | Approve, 12 months  
See Opioid Analgesics IR Quantity Limits Chart (Column C for 1 month supply or Column D for a 3 month supply) | You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:  
- 270 capsules or tablets/month of oxycodone 5 mg, 10 mg, Oxydol 5 mg or 7.5 mg, or RoxyBond 5 mg  
- 180 tablets/month of oxycodone 15 mg, 20 mg or RoxyBond 15 mg  
- 120 tablets/month of oxycodone 30 mg or RoxyBond 30 mg  
You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.  
[Short Description: Over max quantity.]

17. Deny  
RPh Note: For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage. | Approve, 12 months  
See Opioid Analgesics IR Quantity Limits Chart (Column C for 1 month supply or Column D for a 3 month supply) | You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:  
- 180 mL/month of oxycodone 100 mg/5 mL (20 mg/mL) oral concentrate  
- 2700 mL/month of oxycodone 5 mg/5 mL oral solution  
You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.  
[Short Description: Over max quantity.]

18. Deny  
RPh Note: For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage. | Approve, 12 months  
See Opioid Analgesics IR Quantity Limits Chart (Column C for 1 month supply or Column D for a 3 month supply) | You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:  
- 360 tablets/month of oxymorphone 5 mg  
- 180 tablets/month of oxymorphone 10 mg  
You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.  
[Short Description: Over max quantity.]
<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>19. sol 19</td>
<td>Deny</td>
<td>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 300 tablets/month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.</td>
</tr>
</tbody>
</table>
| 20. sol 20 | Deny RPh Note: For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage. | You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:
- 240 tablets/month of Nucynta (tapentadol) 50 mg tablets
- 180 tablets/month of Nucynta (tapentadol) 75 mg tablets
- 120 tablets/month of Nucynta (tapentadol) 100 mg tablets
- 700 mL/month of Nucynta (tapentadol) oral solution
You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. |
| 21. sol 21 | Deny | You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:
- 240 tablets/month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. |
| 22. sol 22 | Deny RPh Note: For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage. | You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:
- 840 mL of codeine sulfate oral solution in a one month period
- 84 tablets of codeine sulfate tablets in a one month period
You have been approved for the maximum quantity that your plan covers for a duration of 1 month. Your request for additional quantities of the requested drug and strength has been denied. |
| 23. sol 23 | Deny RPh Note: For the denial verbiage, only include the requested drug. | You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:
- 1500 mL/month of hydromorphone oral solution
- 180 suppositories/month hydromorphone suppositories
- 270 tablets/month of hydromorphone 2 mg tablets
You have been approved for the maximum quantity that your plan covers for a duration of 1 month. Your request for additional quantities of the requested drug and strength has been denied. |
|   | Remove all the other drugs from the verbiage. | Quantity Limits Chart (Column C) | - 225 tablets/month of hydromorphone 4 mg tablets  
- 90 tablets/month of hydromorphone 8 mg tablets  
You have been approved for the maximum quantity that your plan covers for a duration of 1 month. Your request for additional quantities of the requested drug and strength has been denied. |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>24.</td>
<td>Deny</td>
<td>Approve, 1 month</td>
<td>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 180 tablets/month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 1 month. Your request for additional quantities of the requested drug and strength has been denied.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>See Opioid Analgesics IR Quantity Limits Chart (Column C)</td>
<td>[Short Description: Over max quantity.]</td>
</tr>
</tbody>
</table>
| 25. | Deny | Approve, 1 month | You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:  
- 120 mL of meperidine oral solution in a one month period  
- 24 tablets of meperidine tablets in a one month period  
You have been approved for the maximum quantity that your plan covers for a duration of 1 month. Your request for additional quantities of the requested drug and strength has been denied. |
|   | RPh Note: For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage. | See Opioid Analgesics IR Quantity Limits Chart (Column C) | [Short Description: Over max quantity.] |
| 26. | Deny | Approve, 1 month | You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:  
- 270 mL/month of morphine sulfate 20 mg/mL (100 mg/5 mL) oral concentrate solution  
- 1350 mL/month of morphine sulfate 10 mg/5 mL or 20 mg/5 mL oral solution  
You have been approved for the maximum quantity that your plan covers for a duration of 1 month. Your request for additional quantities of the requested drug and strength has been denied. |
|   | RPh Note: For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage. | See Opioid Analgesics IR Quantity Limits Chart (Column C) | [Short Description: Over max quantity.] |
| 27. | Deny | Approve, 1 month | You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:  
- 270 suppositories/month of morphine sulfate suppository 5 mg, 10 mg, or 20 mg  
- 180 suppositories/month of morphine sulfate suppository 30 mg  
You have been approved for the maximum quantity that your plan covers for a duration of 1 month. Your request for additional quantities of the requested drug and strength has been denied. |
|   | RPh Note: For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage. | See Opioid Analgesics IR Quantity Limits Chart (Column C) | [Short Description: Over max quantity.] |
| 28. | Deny | Approve, 1 month | You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:  
- 270 tablets/month of morphine sulfate 15 mg tablets  
- 180 tablets/month of morphine sulfate 30 mg tablets  
You have been approved for the maximum quantity that your plan covers for a duration of 1 month. Your request for additional quantities of the requested drug and strength has been denied. |
<p>|   | RPh Note: For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage. | See Opioid Analgesics IR Quantity Limits Chart (Column C) | [Short Description: Over max quantity.] |</p>
<table>
<thead>
<tr>
<th></th>
<th>Deny</th>
<th>Approve, 1 month</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>29.</td>
<td>RPh Note: For the denial verbiage, only include the requested drug. Remove all other drugs from the verbiage.</td>
<td>Approve, 1 month</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Quantity Limits Chart (Column C)</td>
<td>Quantity Limits Chart (Column C)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:</td>
<td>You have been approved for the maximum quantity that your plan covers for a duration of 1 month. Your request for additional quantities of the requested drug and strength has been denied.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- 270 capsules or tablets/month of oxycodone 5 mg, 10 mg, Oxyday 5 mg or 7.5 mg, or RoxyBond 5 mg</td>
<td>[Short Description: Over max quantity.]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- 180 tablets/month of oxycodone 15 mg, 20 mg or RoxyBond 15 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- 120 tablets/month of oxycodone 30 mg or RoxyBond 30 mg</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30.</td>
<td>RPh Note: For the denial verbiage, only include the requested drug. Remove all other drugs from the verbiage.</td>
<td>Approve, 1 month</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Quantity Limits Chart (Column C)</td>
<td>Quantity Limits Chart (Column C)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:</td>
<td>You have been approved for the maximum quantity that your plan covers for a duration of 1 month. Your request for additional quantities of the requested drug and strength has been denied.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- 180 mL/month of oxycodone 100 mg/5 mL (20 mg/mL) oral concentrate</td>
<td>[Short Description: Over max quantity.]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- 2700 mL/month of oxycodone 5 mg/5 mL oral solution</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>31.</td>
<td>RPh Note: For the denial verbiage, only include the requested drug. Remove all other drugs from the verbiage.</td>
<td>Approve, 1 month</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Quantity Limits Chart (Column C)</td>
<td>Quantity Limits Chart (Column C)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:</td>
<td>You have been approved for the maximum quantity that your plan covers for a duration of 1 month. Your request for additional quantities of the requested drug and strength has been denied.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- 360 tablets/month of oxymorphone 5 mg</td>
<td>[Short Description: Over max quantity.]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- 180 tablets/month of oxymorphone 10 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>32.</td>
<td></td>
<td>Approve, 1 month</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Quantity Limits Chart (Column C)</td>
<td>Quantity Limits Chart (Column C)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 300 tablets/month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 1 month. Your request for additional quantities of the requested drug and strength has been denied.</td>
<td></td>
<td>[Short Description: Over max quantity.]</td>
</tr>
<tr>
<td></td>
<td>- 240 tablets/month of Nucynta (tapentadol) 50 mg tablets</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- 180 tablets/month of Nucynta (tapentadol) 75 mg tablets</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- 120 tablets/month of Nucynta (tapentadol) 100 mg tablets</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- 700 mL/month of Nucynta (tapentadol) oral solution</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
You have been approved for the maximum quantity that your plan covers for a duration of 1 month. Your request for additional quantities of the requested drug and strength has been denied.

[Short Description: Over max quantity.]

| 34 | Deny | Approve, 1 month | You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 240 tablets/month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 1 month. Your request for additional quantities of the requested drug and strength has been denied.

[Short Description: Over max quantity.] |

### Opioid Analgesics IR Quantity Limits Chart

Coverage is provided without prior authorization (for patients not identified as potential first fills) for a 30-day or 90-day supply of an immediate-release opioid for a quantity that corresponds to ≤ 90 MME/day. Coverage for quantities that correspond to ≤ 200 MME/day for a 30-day or 90-day supply is provided through prior authorization when criteria for approval are met.

These quantity limits should accumulate across all drugs of the same unit limit (i.e., drugs with 30 units accumulate together, drugs with 60 units accumulate together, etc).

<table>
<thead>
<tr>
<th>Drug/Strength**</th>
<th>Labeled Dosing</th>
<th>Initial 1 Month Limit*</th>
<th>Initial 3 Month Limit*</th>
<th>Post 1 Month Limit*</th>
<th>Post 3 Month Limit*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>≤ 90 MME/day (per 25 days)</td>
<td>≤ 90 MME/day (per 75 days)</td>
<td>≤ 200 MME/day (per 25 days)</td>
<td>≤ 200 MME/day (per 75 days)</td>
</tr>
<tr>
<td>Codeine sulfate oral soln 30 mg/5 mL</td>
<td>15 to 60 mg (2.5 mL to 10 mL) q4h. Max Daily Dose 360 mg.</td>
<td>210 mL‡ (27 MME/day)</td>
<td>210 mL‡ (27 MME/day)</td>
<td>840 mL‡ (54 MME/day)</td>
<td>Use Column C</td>
</tr>
<tr>
<td>Codeine sulfate tab 15 mg</td>
<td>15 to 60 mg q4h. Max Daily Dose 360 mg.</td>
<td>42 tabs‡ (13.5 MME/day)</td>
<td>42 tabs‡ (13.5 MME/day)</td>
<td>84 tabs‡ (13.5 MME/day)</td>
<td>Use Column C</td>
</tr>
<tr>
<td>Codeine sulfate tab 30 mg</td>
<td>15 to 60 mg q4h. Max Daily Dose 360 mg.</td>
<td>42 tabs‡ (27 MME/day)</td>
<td>42 tabs‡ (27 MME/day)</td>
<td>84 tabs‡ (27 MME/day)</td>
<td>Use Column C</td>
</tr>
<tr>
<td>Codeine sulfate tab 60 mg</td>
<td>15 to 60 mg q4h. Max Daily Dose 360 mg.</td>
<td>42 tabs‡ (54 MME/day)</td>
<td>42 tabs‡ (54 MME/day)</td>
<td>84 tabs‡ (54 MME/day)</td>
<td>Use Column C</td>
</tr>
<tr>
<td>Hydromorphone oral soln 5 mg/5 mL (1 mg/mL)</td>
<td>2.5 mg – 10 mg (2.5 mL to 10 mL) q3-6h</td>
<td>600 mL (80 MME/day)</td>
<td>1800 mL (80 MME/day)</td>
<td>1500 mL (200 MME/day)</td>
<td>4500 mL (200 MME/day)</td>
</tr>
<tr>
<td>Hydromorphone supp 3 mg</td>
<td>1 supp q6-8h</td>
<td>120 supps (48 MME/day)</td>
<td>360 supps (48 MME/day)</td>
<td>180 supps (72 MME/day)</td>
<td>540 supps (72 MME/day)</td>
</tr>
<tr>
<td>Hydromorphone tab 2 mg</td>
<td>2-4 mg q4-6h</td>
<td>180 tabs (48 MME/day)</td>
<td>540 tabs (48 MME/day)</td>
<td>270 tabs (72 MME/day)</td>
<td>810 tabs (72 MME/day)</td>
</tr>
<tr>
<td>Hydromorphone tab 4 mg</td>
<td>2-4 mg q4-6h</td>
<td>150 tabs (80 MME/day)</td>
<td>450 tabs (80 MME/day)</td>
<td>225 tabs (120 MME/day)</td>
<td>675 tabs (120 MME/day)</td>
</tr>
<tr>
<td>Hydromorphone tab 8 mg</td>
<td>2-4 mg q4-6h</td>
<td>60 tabs (64 MME/day)</td>
<td>180 tabs (64 MME/day)</td>
<td>90 tabs (96 MME/day)</td>
<td>270 tabs (96 MME/day)</td>
</tr>
<tr>
<td>Levorphanol tab 1 mg</td>
<td>1-3 mg q6-8h</td>
<td>120 tabs (44 MME/day)</td>
<td>360 tabs (44 MME/day)</td>
<td>180 tabs (66 MME/day)</td>
<td>540 tabs (66 MME/day)</td>
</tr>
<tr>
<td>Levorphanol tab 2 mg</td>
<td>1-3 mg q6-8h</td>
<td>120 tabs</td>
<td>360 tabs</td>
<td>180 tabs</td>
<td>540 tabs</td>
</tr>
<tr>
<td>Drug</td>
<td>MME/day (90 tabs)</td>
<td>MME/day (180 tabs)</td>
<td>MME/day (90 caps)</td>
<td>MME/day (180 caps)</td>
<td></td>
</tr>
<tr>
<td>------------------------------</td>
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<td>-------------------</td>
<td></td>
</tr>
<tr>
<td>Levothorphanol tab 3 mg</td>
<td>1-3 mg q6-8h</td>
<td>60 tabs (66 MME/day)</td>
<td>180 tabs (198 MME/day)</td>
<td>540 tabs (198 MME/day)</td>
<td></td>
</tr>
<tr>
<td>Meperidine oral soln 50 mg/5 mL</td>
<td>50-150 mg (5-15 mL)</td>
<td>90 mL*** (30 MME/day)</td>
<td>90 mL*** (30 MME/day)</td>
<td>120 mL*** (30 MME/day)</td>
<td></td>
</tr>
<tr>
<td>Meperidine tab 50 mg</td>
<td>50-150 mg q3-4h</td>
<td>18 tabs**** (60 MME/day)</td>
<td>18 tabs**** (60 MME/day)</td>
<td>24 tabs**** (60 MME/day)</td>
<td></td>
</tr>
<tr>
<td>Meperidine tab 100 mg</td>
<td>50-150 mg q3-4h</td>
<td>18 tabs**** (60 MME/day)</td>
<td>18 tabs**** (60 MME/day)</td>
<td>24 tabs**** (60 MME/day)</td>
<td></td>
</tr>
<tr>
<td>Morphine sulfate (conc) oral soln 20 mg/mL</td>
<td>10-20 mg q4h</td>
<td>135 mL (90 MME/day)</td>
<td>405 mL (90 MME/day)</td>
<td>270 mL (180 MME/day)</td>
<td></td>
</tr>
<tr>
<td>Morphine sulfate oral soln 10 mg/5 mL</td>
<td>10-20 mg q4h</td>
<td>900 mL (90 MME/day)</td>
<td>2700 mL (90 MME/day)</td>
<td>1350 mL (180 MME/day)</td>
<td></td>
</tr>
<tr>
<td>Morphine sulfate oral soln 20 mg/5 mL</td>
<td>10-20 mg q4h</td>
<td>675 mL (90 MME/day)</td>
<td>2025 mL (90 MME/day)</td>
<td>1350 mL (180 MME/day)</td>
<td></td>
</tr>
<tr>
<td>Morphine sulfate supp 5 mg</td>
<td>10-20 mg q4h</td>
<td>180 supps (30 MME/day)</td>
<td>540 supps (30 MME/day)</td>
<td>270 supps (45 MME/day)</td>
<td></td>
</tr>
<tr>
<td>Morphine sulfate supp 10 mg</td>
<td>10-20 mg q4h</td>
<td>180 supps (60 MME/day)</td>
<td>540 supps (60 MME/day)</td>
<td>270 supps (90 MME/day)</td>
<td></td>
</tr>
<tr>
<td>Morphine sulfate supp 20 mg</td>
<td>10-20 mg q4h</td>
<td>120 supps (80 MME/day)</td>
<td>360 supps (80 MME/day)</td>
<td>270 supps (180 MME/day)</td>
<td></td>
</tr>
<tr>
<td>Morphine sulfate supp 30 mg</td>
<td>10-20 mg q4h</td>
<td>90 supps (90 MME/day)</td>
<td>270 supps (90 MME/day)</td>
<td>180 supps (180 MME/day)</td>
<td></td>
</tr>
<tr>
<td>Morphine sulfate tab 15 mg</td>
<td>15-30 mg q4h</td>
<td>180 tabs (90 MME/day)</td>
<td>540 tabs (90 MME/day)</td>
<td>270 tabs (135 MME/day)</td>
<td></td>
</tr>
<tr>
<td>Morphine sulfate tab 30 mg</td>
<td>15-30 mg q4h</td>
<td>90 tabs (90 MME/day)</td>
<td>270 tabs (90 MME/day)</td>
<td>180 tabs (180 MME/day)</td>
<td></td>
</tr>
<tr>
<td>Oxycodone cap 5 mg</td>
<td>5-15 mg q4-6h</td>
<td>180 caps (45 MME/day)</td>
<td>540 caps (45 MME/day)</td>
<td>270 caps (67.5 MME/day)</td>
<td></td>
</tr>
<tr>
<td>Oxycodone oral concentrate 100 mg/5 mL</td>
<td>5-15 mg q4-6h</td>
<td>90 mL (90 MME/day)</td>
<td>270 mL (90 MME/day)</td>
<td>180 mL (180 MME/day)</td>
<td></td>
</tr>
<tr>
<td>Oxycodone soln 5 mg/5 mL</td>
<td>5-15 mg q4-6h</td>
<td>900 mL (45 MME/day)</td>
<td>2700 mL (45 MME/day)</td>
<td>2700 mL (135 MME/day)</td>
<td></td>
</tr>
<tr>
<td>Oxycodone oral soln 10 mg/5 mL</td>
<td>5-15 mg q4-6h</td>
<td>180 tabs (45 MME/day)</td>
<td>540 tabs (45 MME/day)</td>
<td>270 tabs (67.5 MME/day)</td>
<td></td>
</tr>
<tr>
<td>Oxycodone tab 5 mg</td>
<td>5-15 mg q4-6h</td>
<td>180 tabs (67.5 MME/day)</td>
<td>540 tabs (67.5 MME/day)</td>
<td>270 tabs (101.25 MME/day)</td>
<td></td>
</tr>
<tr>
<td>Oxycodone tab 10 mg</td>
<td>5-15 mg q4-6h</td>
<td>180 tabs (90 MME/day)</td>
<td>540 tabs (90 MME/day)</td>
<td>270 tabs (135 MME/day)</td>
<td></td>
</tr>
<tr>
<td>Oxycodone tab 15 mg</td>
<td>5-15 mg q4-6h</td>
<td>180 tabs (90 MME/day)</td>
<td>540 tabs (90 MME/day)</td>
<td>270 tabs (135 MME/day)</td>
<td></td>
</tr>
<tr>
<td>Oxycodone tab 20 mg</td>
<td>5-15 mg q4-6h</td>
<td>180 tabs (90 MME/day)</td>
<td>540 tabs (90 MME/day)</td>
<td>270 tabs (135 MME/day)</td>
<td></td>
</tr>
<tr>
<td>Oxycodone tab 30 mg</td>
<td>5-15 mg q4-6h</td>
<td>180 tabs (90 MME/day)</td>
<td>540 tabs (90 MME/day)</td>
<td>270 tabs (135 MME/day)</td>
<td></td>
</tr>
<tr>
<td>Oxymorphone tab 5 mg</td>
<td>10-20 mg q4-6h</td>
<td>180 tabs (90 MME/day)</td>
<td>540 tabs (90 MME/day)</td>
<td>360 tabs (90 MME/day)</td>
<td></td>
</tr>
<tr>
<td>Oxymorphone tab 10 mg</td>
<td>10-20 mg q4-6h</td>
<td>90 tabs (90 MME/day)</td>
<td>270 tabs (90 MME/day)</td>
<td>180 tabs (180 MME/day)</td>
<td></td>
</tr>
<tr>
<td>Opioids IR - 7-Day Acute Pain Duration Limit with MME Limit and Post Limit 2221-M 01-2019 (2)</td>
<td>©2019 CVS Caremark. All rights reserved.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pentazocine/naloxone 50/0.5 mg</td>
<td>1-2 tabs q3-4h. Total daily dose should not exceed 12 tablets.</td>
<td>120 tabs*** (74 MME/day)</td>
<td>120 tabs*** (74 MME/day)</td>
<td>300 tabs*** (185 MME/day)</td>
<td>Use Column C</td>
</tr>
<tr>
<td>RoxyBond 5 mg</td>
<td>5-15 mg q4-6h</td>
<td>180 tabs (45 MME/day)</td>
<td>540 tabs (45 MME/day)</td>
<td>270 tabs (67.5 MME/day)</td>
<td>810 tabs (67.5 MME/day)</td>
</tr>
<tr>
<td>RoxyBond 15 mg</td>
<td>5-15 mg q4-6h</td>
<td>120 tabs (90 MME/day)</td>
<td>360 tabs (90 MME/day)</td>
<td>180 tabs (135 MME/day)</td>
<td>540 tabs (135 MME/day)</td>
</tr>
<tr>
<td>RoxyBond 30 mg</td>
<td>5-15 mg q4-6h</td>
<td>60 tabs (90 MME/day)</td>
<td>180 tabs (90 MME/day)</td>
<td>120 tabs (180 MME/day)</td>
<td>360 tabs (180 MME/day)</td>
</tr>
<tr>
<td>Tapentadol oral soln 20 mg/mL†</td>
<td>50 mg (2.5 mL) to 100 mg (5 mL) every 4 to 6 hours. Max daily dose is 700 mg on the first day and 600 mg on subsequent days.</td>
<td>300 mL (80 MME/day)</td>
<td>900 mL (80 MME/day)</td>
<td>700 mL (186.7 MME/day)</td>
<td>2100 mL (186.7 MME/day)</td>
</tr>
<tr>
<td>Tapentadol tab 50 mg</td>
<td>50 mg, 75 mg, or 100 mg every 4 to 6 hours. Max daily dose is 700 mg on the first day and 600 mg on subsequent days.</td>
<td>120 tabs (80 MME/day)</td>
<td>360 tabs (80 MME/day)</td>
<td>240 tabs (160 MME/day)</td>
<td>720 tabs (160 MME/day)</td>
</tr>
<tr>
<td>Tapentadol tab 75 mg</td>
<td>50 mg, 75 mg, or 100 mg every 4 to 6 hours. Max daily dose is 700 mg on the first day and 600 mg on subsequent days.</td>
<td>90 tabs (90 MME/day)</td>
<td>270 tabs (90 MME/day)</td>
<td>180 tabs (180 MME/day)</td>
<td>540 tabs (180 MME/day)</td>
</tr>
<tr>
<td>Tapentadol tab 100 mg</td>
<td>50 mg, 75 mg, or 100 mg every 4 to 6 hours. Max daily dose is 700 mg on the first day and 600 mg on subsequent days.</td>
<td>60 tabs (80 MME/day)</td>
<td>180 tabs (80 MME/day)</td>
<td>120 tabs (160 MME/day)</td>
<td>360 tabs (160 MME/day)</td>
</tr>
<tr>
<td>Tramadol 50 mg</td>
<td>50-100 mg q4-6h, MAX = 400 mg/day</td>
<td>180 tabs (30 MME/day)</td>
<td>540 tabs (30 MME/day)</td>
<td>240 tabs (40 MME/day)</td>
<td>720 tabs (40 MME/day)</td>
</tr>
</tbody>
</table>

*The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing. Limits are set up as quantity versus time edits.

**The limit criteria apply to both brand and generic, if available.

***This drug is indicated for short-term acute use; therefore, the 30-day limit will be the same as the 90-day limit.

****Due to risk of accumulation, the 30-day and 90-day initial limit allows a quantity that corresponds to a 3-day supply only and the 30-day and 90-day post limit allows a quantity that corresponds to a 4-day supply only.

†Available in 100 mL and 200 mL bottles. It is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

‡This drug is indicated for short-term acute use; therefore, the 30-day limit will be the same as the 90-day limit. The initial quantity limit for codeine will be set at a quantity that corresponds to a one week supply. The post limit quantity will be set at a quantity that corresponds to a two week supply.
# DURATION LIMIT CRITERIA

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>ACETAMINOPHEN/ASPIRIN/IBUPROFEN CONTAINING OPIOID ANALGESICS (BRAND AND GENERIC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(generic)*</td>
<td>(acetaminophen and benzhydrocodone)</td>
</tr>
<tr>
<td></td>
<td>(acetaminophen and codeine)</td>
</tr>
<tr>
<td></td>
<td>(acetaminophen and hydrocodone)</td>
</tr>
<tr>
<td></td>
<td>(acetaminophen and oxycodone)</td>
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<tr>
<td></td>
<td>(acetaminophen and tramadol)</td>
</tr>
<tr>
<td></td>
<td>(acetaminophen, caffeine, and dihydrocodeine)</td>
</tr>
<tr>
<td></td>
<td>(aspirin and oxycodone)</td>
</tr>
<tr>
<td></td>
<td>(aspirin, caffeine, and dihydrocodeine)</td>
</tr>
<tr>
<td></td>
<td>(ibuprofen and hydrocodone)</td>
</tr>
<tr>
<td></td>
<td>(ibuprofen and oxycodone)</td>
</tr>
</tbody>
</table>

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* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

**1358-E may be used as a stand-alone criteria OR in combination with Opioids IR APAP-ASA-IBU Combo Products Limit 1365-H. The Opioids IR APAP-ASA-IBU Combo Products Limit 1365-H will be coded separately.

## FDA-APPROVED INDICATIONS

**Acetaminophen/Caffeine/Dihydrocodeine**

Acetaminophen/caffeine/dihydrocodeine bitartrate tablets are indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

### Limitations of Use

- Because of the risks of addiction, abuse, and misuse, with opioids, even at recommended doses, reserve acetaminophen/caffeine/dihydrocodeine bitartrate tablets for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]:
  - Have not been tolerated, or are not expected to be tolerated,
  - Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

**Aspirin/Caffeine/Dihydrocodeine**

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For the relief of moderate to moderately severe pain.

**Benzhydrocodone/Acetaminophen (Apadaz)**

Apadaz is indicated for the short-term (no more than 14 days) management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

**Limitations of Use**

Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve Apadaz for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]:

- Have not been tolerated, or are not expected to be tolerated,
- Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

**Codeine/Acetaminophen**

Oral Solution and Tablets

Acetaminophen and codeine phosphate oral solution and tablets are indicated for the management of mild to moderate pain, where treatment with an opioid is appropriate and for which alternative treatments are inadequate.

**Limitations of Use**

Because of the risks of addiction, abuse, and misuse, with opioids, even at recommended doses, reserve acetaminophen and codeine phosphate oral solution, suspension, and tablets for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]:

- Have not provided adequate analgesia, or are not expected to provide adequate analgesia,
- Have not been tolerated, or are not expected to be tolerated.

**Hydrocodone/Acetaminophen**

Hydrocodone bitartrate and acetaminophen is indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

**Limitations of Use**

- Because of the risks of addiction, abuse, and misuse, with opioids, even at recommended doses, reserve hydrocodone bitartrate and acetaminophen for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]:
  - Have not been tolerated, or are not expected to be tolerated,
  - Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

**Hydrocodone/Ibuprofen**

Hydrocodone bitartrate and ibuprofen tablets are indicated for the short-term management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

**Limitations of Use**

- Carefully consider the potential benefits and risks of hydrocodone bitartrate and ibuprofen tablets and other treatment options before deciding to use hydrocodone bitartrate and ibuprofen tablets. Use the lowest effective dosage for the shortest duration consistent with individual treatment goals. Do not use hydrocodone bitartrate and ibuprofen tablets for the treatment of conditions such as osteoarthritis or rheumatoid arthritis.
- Because of the risks of addiction, abuse, and misuse, with opioids, even at recommended doses, reserve hydrocodone bitartrate and ibuprofen tablets for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]:
  - Have not been tolerated, or are not expected to be tolerated,
  - Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

**Oxycodone/Acetaminophen**

Oxycodone and acetaminophen is indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

**Limitations of Use**

- Because of the risks of addiction, abuse, and misuse, with opioids, even at recommended doses, reserve oxycodone and acetaminophen for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]:

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Have not been tolerated, or are not expected to be tolerated,
• Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

Oxycodone/Aspirin
Oxycodone and aspirin tablets are indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

Limitations of Use
• Because of the risks of addiction, abuse, and misuse, with opioids, even at recommended doses, reserve oxycodone and aspirin tablets for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]:
  • Have not been tolerated, or are not expected to be tolerated,
  • Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

Oxycodone/Ibuprofen
Oxycodone hydrochloride and ibuprofen tablets are indicated for the management of short term (no more than 7 days) acute to moderate pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

Limitations of Use
• Carefully consider the potential benefits and risks of Oxycodone Hydrochloride and Ibuprofen Tablets and other treatment options before deciding to use Oxycodone Hydrochloride and Ibuprofen Tablets. Use the lowest effective dose for the shortest duration consistent with individual treatment goals.
• Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve Oxycodone Hydrochloride and Ibuprofen tablets for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]:
  • Have not been tolerated, or are not expected to be tolerated,
  • Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

Tramadol/Acetaminophen
Ultracet (tramadol/acetaminophen) tablets are indicated for the management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

Limitations of Use
• Ultracet (tramadol/acetaminophen) tablets are indicated for short-term use of five days or less.
• Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve Ultracet (tramadol/acetaminophen) for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]:
  • Have not been tolerated, or are not expected to be tolerated,
  • Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

For hydrocodone/ibuprofen tablets, oxycodone/ibuprofen tablets, tramadol/acetaminophen tablets:
• The patient will not require use of MORE than the plan allowance of any of the following: A) 50 tablets/month of hydrocodone/ibuprofen tablets, B) 28 tablets/month of oxycodone/ibuprofen tablets, C) 40 tablets/month of tramadol/acetaminophen tablets

For acetaminophen/caffeine, acetaminophen/codeine, acetaminophen/hydrocodone, acetaminophen/oxycodone, acetaminophen/codeine/dihydrocodeine, aspirin/oxycodone, aspirin/caffeine/dihydrocodeine:
• The requested drug is being prescribed for pain associated with cancer, sickle cell disease, a terminal condition, or pain being managed through hospice or palliative care

OR
• The requested drug is being prescribed for moderate to severe CHRONIC pain where use of an opioid analgesic is appropriate. [Note: Chronic pain is generally defined as pain that typically lasts greater than 3 months.]

OR
• The patient requires extended treatment beyond 7 days for ongoing management of ACUTE pain
Quantity Limits may apply.

**RATIONALE**

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Acetaminophen/caffeine/dihydrocodeine, hydrocodone/acetaminophen, oxycodone/acetaminophen, and oxycodone/ibuprofen are indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. Aspirin/caffeine/dihydrocodeine is indicated for the relief of moderate to moderately severe pain. Codeine and acetaminophen is indicated for the management of mild to moderate pain, where treatment with an opioid is appropriate and for which alternative treatments are inadequate. Hydrocodone/ibuprofen containing opioid analgesics are indicated for the short-term management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. Oxycodone/ibuprofen tablets are indicated for the management of short-term (no more than 7 days) acute to moderate pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. Ultracet (tramadol/acetaminophen) is indicated for the management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. Apadaz (benzhydrocodone/acetaminophen) is indicated for the short-term (no more than 14 days) management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve immediate-release combination product opioids for use in patients for whom alternative treatment options (e.g., non-opioid analgesics) 1) have not been tolerated or are not expected to be tolerated, or 2) have not provided adequate analgesia or are not expected to provide adequate analgesia.1-23

If the patient has filled a prescription for at least a 1-day supply of a drug indicating the patient is being treated for cancer or sickle cell disease (SCD) within the past 365 days under a prescription benefit administered by CVS Caremark, then 1) when using this program in combination with Opioids IR APAP-ASA-IBU Combo Products Limit 1365-H, the claim will proceed to the subsequent initial quantity limit criteria (1365-H) OR 2) when using this as a stand-alone program, the requested drug will be paid under that prescription benefit.

If a claim is submitted with an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care under a prescription benefit administered by CVS Caremark, then 1) when using this program in combination with Opioids IR APAP-ASA-IBU Combo Products Limit 1365-H, the claim will proceed to the subsequent initial quantity limit criteria (1365-H) OR 2) when using this as a stand-alone program, the requested drug will be paid under that prescription benefit.

If the patient has an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in their member health profile in the past 365 days, then 1) when using this program in combination with Opioids IR APAP-ASA-IBU Combo Products Limit 1365-H, the claim will proceed to the subsequent initial quantity limit criteria (1365-H) OR 2) when using this as a stand-alone program, the requested drug will be paid under that prescription benefit.

If a claim is submitted using a hospice patient residence code under a prescription benefit administered by CVS Caremark, then 1) when using this program in combination with Opioids IR APAP-ASA-IBU Combo Products Limit 1365-H, the claim will proceed to the subsequent initial quantity limit criteria (1365-H) OR 2) when using this as a stand-alone program, the requested drug will be paid under that prescription benefit.

For patients with no prescription claims of a cancer drug or a sickle cell disease drug in the past 365 days, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care submitted with their prescription claim, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in the member health profile in the past 365 days, or no hospice patient residence code submitted with their prescription claim:
If the patient has filled a prescription for at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history in the past 90 days under a prescription benefit administered by CVS Caremark, then 1) when using this program in combination with Opioids IR APAP-ASA-IBU Combo Products Limit 1365-H, the claim will proceed to the subsequent initial quantity limit criteria (1365-H) OR 2) when using this as a stand-alone program, the requested drug will be paid under that prescription benefit.

If the patient does not have at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history in the past 90 days (i.e., this is the patient’s first fill of an opioid), and the incoming prescription drug is being filled for more than a 7-day supply, then the claim will reject with a message indicating that the patient can receive a 7-day supply or submit a prior authorization (PA). The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit. If using this program in combination with Opioids IR APAP-ASA-IBU Combo Products Limit 1365-H, the claim will proceed to the subsequent initial quantity limits would apply. If the incoming prescription drug is being filled for less than a 7-day supply, then 1) when using this program in combination with Opioids IR APAP-ASA-IBU Combo Products Limit 1365-H, the claim will proceed to the subsequent initial quantity limit criteria (1365-H) OR 2) when using this as a stand-alone program, the requested drug will be paid under that prescription benefit.

The Centers for Disease and Prevention (CDC) Guideline for Prescribing Opioids for Chronic Pain provides recommendations for primary care clinicians who are prescribing opioids for chronic pain outside of active cancer treatment, sickle cell disease, palliative care, and end-of-life care.24 The National Comprehensive Cancer Network (NCCN) guidelines for Adult Cancer Pain recommend for continuous pain, it is appropriate to give pain medication on a regular schedule with supplemental doses for breakthrough pain. Add an extended-release or long-acting formulation to provide background analgesia for control of chronic persistent pain controlled on stable doses of short-acting opioids. When possible, use the same opioid for short-acting and extended-release forms. Allow rescue doses of short-acting opioids up to every 1 hour as needed.25 The NCCN Palliative Care pain management recommendation is to treat according to NCCN guidelines for adult cancer pain management.25 For patients with no prescription claims of a cancer drug in the past 365 days, no ICD 10 diagnosis code indicating cancer or palliative care submitted with their prescription claim, no ICD 10 diagnosis code indicating cancer or palliative care in the member health profile in the past 365 days, or no hospice patient residence code submitted with their prescription claim who are identified through the prior authorization criteria as having cancer, a terminal condition, or pain being managed through hospice or palliative care, acute pain duration limits will not apply (except if the request is for hydrocodone/ibuprofen tablets, oxycodone/ibuprofen tablets, tramadol/acetaminophen tablets due to maximum duration specified in product labeling). If using this program in combination with Opioids IR APAP-ASA-IBU Combo Products Limit 1365-H, then subsequent initial quantity limits would apply to all patients regardless of concomitant conditions (e.g., active cancer treatment, palliative care, and end-of-life care) due to the non-opioid components.

According to the National Heart, Lung, and Blood Institute’s (NHLBI) guidelines for Sickle Cell Disease (SCD), pain is the most common symptom of SCD. Pain can be acute, chronic, or an acute episode superimposed on chronic pain. Recurrent acute pain crises (also known as vaso-occlusive crises) are the most common manifestation of SCD. Chronic pain is also one of the most common chronic complications of SCD. Pain management must be guided by patient report of severity. No biomarkers or imaging studies can validate pain or assess its severity. Medications used to treat SCD-related pain should be tailored to the individual. For pain that is not relieved by nonsteroidal anti-inflammatory drugs (NSAIDs) or other measures, either short-acting or long-acting opioids may be used to manage pain in SCD.27 For patients with no prescription claims of a sickle cell disease drug in the past 365 days, no ICD 10 diagnosis code indicating sickle cell disease submitted with their prescription claim, or no ICD 10 diagnosis code indicating sickle cell disease in the member health profile in the past 365 days who are identified through the prior authorization criteria as having sickle cell disease, acute pain duration limits will not apply (except if the request is for hydrocodone/ibuprofen tablets, oxycodone/ibuprofen tablets, tramadol/acetaminophen tablets due to maximum duration specified in product labeling). If using this program in combination with Opioids IR APAP-ASA-IBU Combo Products Limit 1365-H, then...
subsequent initial quantity limits would apply to all patients regardless of concomitant conditions (e.g., sickle cell disease) due to the non-opioid components.

According to the Center for Disease Control (CDC) Guideline for Prescribing Opioids for Chronic Pain, long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should not prescribe a greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed. Coverage is provided for up to 7 days initially to provide an amount sufficient for the treatment of acute pain.

The quantities of 28 tablets/month of oxycodone/ibuprofen tablets, 40 tablets/month of tramadol/acetaminophen tablets, or 50 tablets/month of hydrocodone/ibuprofen tablets are provided upon approval of the PA to allow coverage consistent with product labeling.

For the short-term (generally less than 10 days) management of acute pain, the recommended dose of all strengths of hydrocodone bitartrate/ibuprofen is one tablet every four to six hours as necessary. Dosages should not exceed five tablets in a 24-hour period. Since hydrocodone bitartrate/ibuprofen is only indicated for short-term use, the criteria allow for a quantity sufficient for a 10-day supply (50 tablets).

For the management of acute to moderate pain severe enough to require an opioid analgesic, the recommended dose of oxycodone and ibuprofen is one tablet every 6 hours as needed for pain. Dosage should not exceed 4 tablets in a 24-hour period and should not exceed 7 days. Since oxycodone/ibuprofen is only indicated for short-term use, the criteria allow for a quantity sufficient for a 7-day supply (28 tablets).

For the short-term (five days or less) management of acute pain, the recommended dose of Ultracet is 2 tablets every 4 to 6 hours as needed for pain relief, up to a maximum of 8 tablets per day. Since Ultracet is only indicated for short-term use, the criteria allow for a quantity sufficient for a 5-day supply (40 tablets).

PROGRAM DESCRIPTION**

Acute pain duration limits do not apply if the patient has a drug in claims history in the past year that indicates the patient is being treated for cancer or sickle cell disease. In addition, acute pain duration limits will not apply if a prescription claim is submitted with an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care, if the patient has an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in their member health profile in the past 365 days, or if a prescription claim is submitted using a hospice patient residence code. When using this program in combination with Opioids IR APAP-ASA-IBU Combo Products Limit 1365-H, the subsequent initial quantity limits from the Opioids IR APAP-ASA-IBU Combo Products Limit 1365-H would then apply to all patients regardless of concomitant conditions (e.g., active cancer treatment, palliative care, and end-of-life care) due to the non-opioid components.

When using this as a stand-alone program, the requested drug will be paid under that prescription benefit.

If the patient has filled a prescription for at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history in the past 90 days under a prescription benefit administered by CVS Caremark, then 1) when using this program in combination with Opioids IR APAP-ASA-IBU Combo Products Limit 1365-H, the claim will proceed to the subsequent initial quantity limit criteria (1365-H) OR 2) when using this as a stand-alone program, the requested drug will be paid under that prescription benefit.

If the patient does not have at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history in the past 90 days (i.e., this is the patient’s first fill of an opioid), then coverage is provided for up to a 7-day supply of the immediate-release combination product opioid. Prior

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authorization review is required to determine coverage for a quantity necessary for treatment beyond 7 days. For patients with no prescription claims of a cancer drug or a sickle cell disease drug in the past 365 days, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care submitted with their prescription claim, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in the member health profile in the past 365 days, or no hospice patient residence code submitted with their prescription claim who are identified through the prior authorization criteria as having cancer, sickle cell disease, a terminal condition, or pain being managed through hospice or palliative care, acute pain duration limits will not apply. If using this program in combination with Opioids IR APAP-ASA-IBU Combo Products Limit 1365-H, then subsequent initial quantity limits would apply to all patients regardless of concomitant conditions (e.g., active cancer treatment, sickle cell disease, palliative care, and end-of-life care) due to the non-opioid components.

For hydrocodone/ibuprofen tablets, oxycodone/ibuprofen tablets, tramadol/acetaminophen tablets:
A quantity of 28 tablets/month of oxycodone/ibuprofen tablets, 40 tablets/month of tramadol/acetaminophen tablets, or 50 tablets/month of hydrocodone/ibuprofen tablets is provided upon approval of the PA to allow coverage consistent with product labeling.

**1358-E may be used as a stand-alone criteria OR in combination with Opioids IR APAP-ASA-IBU Combo Products Limit 1365-H.

REFERENCES
INITIAL STEP THERAPY

If the patient has filled a prescription for at least a 1-day supply of a drug indicating the patient is being treated for cancer or sickle cell disease within the past 365 days under a prescription benefit administered by CVS Caremark, then 1) when using this program in combination with Opioids IR APAP-ASA-IBU Combo Products Limit 1365-H, the claim will proceed to the subsequent initial quantity limit criteria (1365-H) OR 2) when using this as a stand-alone program, the requested drug will be paid under that prescription benefit.

If a claim is submitted with an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care under a prescription benefit administered by CVS Caremark, then 1) when using this program in combination with Opioids IR APAP-ASA-IBU Combo Products Limit 1365-H, the claim will proceed to the subsequent initial quantity limit criteria (1365-H) OR 2) when using this as a stand-alone program, the requested drug will be paid under that prescription benefit.

If the patient has an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in their member health profile in the past 365 days, then 1) when using this program in combination with Opioids IR APAP-ASA-IBU Combo Products Limit 1365-H, the claim will proceed to the subsequent initial quantity limit criteria (1365-H) OR 2) when using this as a stand-alone program, the requested drug will be paid under that prescription benefit.

If a claim is submitted using a hospice patient residence code under a prescription benefit administered by CVS Caremark, then 1) when using this program in combination with Opioids IR APAP-ASA-IBU Combo Products Limit 1365-H, the claim will proceed to the subsequent initial quantity limit criteria (1365-H) OR 2) when using this as a stand-alone program, the requested drug will be paid under that prescription benefit.

For patients with no prescription claims of a cancer drug or a sickle cell disease drug in the past 365 days, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care submitted with their prescription claim, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in the member health profile in the past 365 days, or no hospice patient residence code submitted with their prescription claim:
If the patient has filled a prescription for at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history in the past 90 days under a prescription benefit administered by CVS Caremark, then 1) when using this program in combination with Opioids IR APAP-ASA-IBU Combo Products Limit 1365-H, the claim will proceed to the subsequent initial quantity limit criteria (1365-H) OR 2) when using this as a stand-alone program, the requested drug will be paid under that prescription benefit.

If the patient does not have at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history in the past 90 days (i.e., this is the patient’s first fill of an opioid), and the incoming prescription drug is being filled for more than a 7-day supply, then the claim will reject with a message indicating that the patient can receive a 7-day supply or submit a prior authorization (PA). The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit. If using this program in combination with Opioids IR APAP-ASA-IBU Combo Products Limit 1365-H, then subsequent initial quantity limits would apply. If the incoming prescription drug is being filled for less than a 7-day supply, then 1) when using this program in combination with Opioids IR APAP-ASA-IBU Combo Products Limit 1365-H, the claim will proceed to the subsequent initial quantity limit criteria (1365-H) OR 2) when using this as a stand-alone program, the requested drug will be paid under that prescription benefit.

**LIMIT CRITERIA (DAY SUPPLY)**

Acute pain duration limits do not apply if the patient has a drug in claims history in the past year that indicates the patient is being treated for cancer or sickle cell disease. In addition, acute pain duration limits will not apply if a prescription claim is submitted with an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care, if the patient has an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in their member health profile in the past 365 days, or if a prescription claim is submitted using a hospice patient residence code. When using this program in combination with Opioids IR APAP-ASA-IBU Combo Products Limit 1365-H, the claim will proceed to the subsequent initial quantity limit criteria (1365-H) OR when using this as a stand-alone program, the requested drug will be paid under that prescription benefit.

If the patient has filled a prescription for at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history in the past 90 days under a prescription benefit administered by CVS Caremark, then 1) when using this program in combination with Opioids IR APAP-ASA-IBU Combo Products Limit 1365-H, the claim will proceed to the subsequent initial quantity limit criteria (1365-H) OR 2) when using this as a stand-alone program, the requested drug will be paid under that prescription benefit.

If the patient does not have at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history in the past 90 days (i.e., this is the patient’s first fill of an opioid), and the incoming prescription drug is being filled for more than a 7-day supply, then the claim will reject with a message indicating that the patient can receive a 7-day supply or submit a prior authorization (PA) for additional days supply. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit. If using this program in combination with Opioids IR APAP-ASA-IBU Combo Products Limit 1365-H, then subsequent initial quantity limits would apply. If the incoming prescription drug is being filled for less than a 7-day supply, then 1) when using this program in combination with Opioids IR APAP-ASA-IBU Combo Products Limit 1365-H, the claim will proceed to the subsequent initial quantity limit criteria (1365-H) OR 2) when using this as a stand-alone program, the requested drug will be paid under that prescription benefit.

For hydrocodone/ibuprofen tablets, oxycodone/ibuprofen tablets, tramadol/acetaminophen tablets:
A quantity of 28 tablets/month of oxycodone/ibuprofen tablets, 40 tablets/month of tramadol/acetaminophen tablets, or 50 tablets/month of hydrocodone/ibuprofen tablets is provided upon approval of the PA to allow coverage consistent with product labeling.
**1358-E may be used as a stand-alone criteria OR in combination with Opioids IR APAP-ASA-IBU Combo Products Limit 1365-H. The Opioids IR APAP-ASA-IBU Combo Products Limit 1365-H will be coded separately.**

---

### CRITERIA FOR APPROVAL

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1</strong></td>
<td>Is one of the following opioid combination products (brand or generic) being requested: A) hydrocodone/IBUPROFEN tablets, B) oxycodone/IBUPROFEN tablets, C) tramadol/ACETAMINOPHEN tablets? [If yes, then skip to question 5.]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

| **2** | Is the requested drug being prescribed for pain associated with cancer, sickle cell disease, a terminal condition, or pain being managed through hospice or palliative care? [If yes, then no further questions.] |
|   | Yes | No |

| **3** | Is the requested drug being prescribed for moderate to severe CHRONIC pain where use of an opioid analgesic is appropriate? [Note: Chronic pain is generally defined as pain that typically lasts greater than 3 months.] [If yes, then no further questions.] |
|   | Yes | No |

| **4** | Does the patient require extended treatment beyond 7 days for ongoing management of ACUTE pain? [No further questions.] |
|   | Yes | No |

| **5** | Does the patient require use of MORE than the plan allowance of any of the following: A) 50 tablets/month of hydrocodone/IBUPROFEN tablets, B) 28 tablets/month of oxycodone/IBUPROFEN tablets, C) 40 tablets/month of tramadol/ACETAMINOPHEN tablets? [RPh Note: If yes, then deny and enter a partial approval for 50 tablets/month of hydrocodone/ibuprofen tablets, B) 28 tablets/month of oxycodone/ibuprofen tablets, C) 40 tablets/month of tramadol/acetaminophen tablets.] |
|   | Yes | No |

---

### Mapping Instructions

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
<th>DENIAL REASONS – DO NOT USE FOR MEDICARE PART D</th>
</tr>
</thead>
</table>
| 1.   |     | Go to 5
| 2.   |     | Go to 2
| 2.   | Approve, 12 months | Go to 3
| 3.   | Approve, 12 months | Go to 4
| 4.   | Approve, 1 month | Deny |

You do not meet the requirements of your plan. Your plan covers this drug when you have one of these conditions:
- Pain due to cancer, sickle cell disease, or a terminal condition
- Pain being managed through hospice or palliative care
- Moderate to severe chronic pain that requires treatment with an opioid

---

**Opioids IR - 7-Day APAP-ASA-IBU Combo Products - Acute Pain Duration Limit 1358-E 01-2019 (2)** ©2019 CVS Caremark. All rights reserved.

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<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>Deny RPh Note: For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.</td>
<td>Approve, 1 month - 50 tablets/month of hydrocodone/ibuprofen tablets or - 28 tablets/month of oxycodone/ibuprofen tablets or - 40 tablets/month of tramadol/APAP tablets</td>
</tr>
</tbody>
</table>

- Acute pain that requires treatment with an opioid for more than seven days
Your request has been denied based on the information we have.

[Short Description: No approvable diagnosis.]

You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:
- 50 tablets/month of hydrocodone/ibuprofen tablets
- 28 tablets/month of oxycodone/ibuprofen tablets
- 40 tablets/month of tramadol/acetaminophen tablets
You have been approved for the maximum quantity that your plan covers for a duration of 1 month. Your request for additional quantities of the requested drug and strength has been denied.

[Short Description: Over max quantity.]
## QUANTITY LIMIT CRITERIA

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>ACETAMINOPHEN/ASPIRIN/IBUPROFEN CONTAINING OPIOID ANALGESICS (generic)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(acetaminophen and benzhydrocodone)</td>
</tr>
<tr>
<td></td>
<td>(acetaminophen and codeine)</td>
</tr>
<tr>
<td></td>
<td>(acetaminophen and hydrocodone)</td>
</tr>
<tr>
<td></td>
<td>(acetaminophen and oxycodone)</td>
</tr>
<tr>
<td></td>
<td>(acetaminophen and tramadol)</td>
</tr>
<tr>
<td></td>
<td>(acetaminophen, caffeine, and dihydrocodeine)</td>
</tr>
<tr>
<td></td>
<td>(aspirin and oxycodone)</td>
</tr>
<tr>
<td></td>
<td>(aspirin, caffeine, and dihydrocodeine)</td>
</tr>
<tr>
<td></td>
<td>(ibuprofen and hydrocodone)</td>
</tr>
<tr>
<td></td>
<td>(ibuprofen and oxycodone)</td>
</tr>
</tbody>
</table>

**Status:** CVS Caremark Criteria  
**Type:** Quantity Limit  
**Ref # 1365-H**

Please note that Xartemis XR is on a separate criteria.  
* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

**1365-H may be used as a stand-alone criteria OR in combination with Opioids IR APAP-ASA-IBU Combo Products – Acute Pain Duration Limit 1358-E. The Opioids IR APAP-ASA-IBU Combo Products – Acute Pain Duration Limit 1358-E will be coded separately.**

### FDA-APPROVED INDICATIONS

**Acetaminophen/Caffeine/Dihydrocodeine**

Acetaminophen/caffeine/dihydrocodeine bitartrate tablets are indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

**Limitations of Use**

- Because of the risks of addiction, abuse, and misuse, with opioids, even at recommended doses, reserve acetaminophen/caffeine/dihydrocodeine bitartrate tablets for use in patients for whom alternative treatment options (e.g., non-opioid analgesics):
  - Have not been tolerated, or are not expected to be tolerated,
Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

**Aspirin/Caffeine/Dihydrocodeine**

For the relief of moderate to moderately severe pain.

**Benzhydrocodone/Acetaminophen (Apadaz)**

Apadaz is indicated for the short-term (no more than 14 days) management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

**Limitations of Use**

Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve Apadaz for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]:

- Have not been tolerated, or are not expected to be tolerated,
- Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

**Hydrocodone/Acetaminophen**

Hydrocodone bitartrate and acetaminophen is indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

**Limitations of Use**

- Because of the risks of addiction, abuse, and misuse, with opioids, even at recommended doses, reserve hydrocodone bitartrate and acetaminophen for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]:
  - Have not provided adequate analgesia, or are not expected to provide adequate analgesia,
  - Have not been tolerated, or are not expected to be tolerated.

**Hydrocodone/Ibuprofen**

Hydrocodone bitartrate and ibuprofen tablets are indicated for the short-term management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

**Limitations of Use**

- Carefully consider the potential benefits and risks of hydrocodone bitartrate and ibuprofen tablets and other treatment options before deciding to use hydrocodone bitartrate and ibuprofen tablets. Use the lowest effective dosage for the shortest duration consistent with individual treatment goals. Do not use hydrocodone bitartrate and ibuprofen tablets for the treatment of conditions such as osteoarthritis or rheumatoid arthritis.

- Because of the risks of addiction, abuse, and misuse, with opioids, even at recommended doses, reserve hydrocodone bitartrate and ibuprofen tablets for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]:
  - Have not been tolerated, or are not expected to be tolerated,
  - Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

**Oxycodone/Acetaminophen**

Oxycodone and acetaminophen is indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

**Limitations of Use**

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• Because of the risks of addiction, abuse, and misuse, with opioids, even at recommended doses, reserve oxycodone and acetaminophen for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]:
  o Have not been tolerated, or are not expected to be tolerated,
  o Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

Oxycodone/Aspirin
Oxycodone and aspirin tablets are indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

Limitations of Use
• Because of the risks of addiction, abuse, and misuse, with opioids, even at recommended doses, reserve oxycodone and aspirin tablets for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]:
  o Have not been tolerated, or are not expected to be tolerated,
  o Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

Oxycodone/Ibuprofen
Oxycodone hydrochloride and ibuprofen tablets are indicated for the management of short term (no more than 7 days) acute to moderate pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

Limitations of Use
• Carefully consider the potential benefits and risks of Oxycodone Hydrochloride and Ibuprofen Tablets and other treatment options before deciding to use Oxycodone Hydrochloride and Ibuprofen Tablets. Use the lowest effective dose for the shortest duration consistent with individual treatment goals.
• Because of the risks of addiction, abuse, and misuse, with opioids, even at recommended doses, reserve Oxycodone Hydrochloride and Ibuprofen tablets for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]:
  o Have not been tolerated, or are not expected to be tolerated,
  o Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

Tramadol/Acetaminophen
Ultracet (tramadol/acetaminophen) tablets are indicated for the management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

Limitations of Use
• Ultracet (tramadol/acetaminophen) tablets are indicated for short-term use of five days or less.
• Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve Ultracet (tramadol/acetaminophen) for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]:
  o Have not been tolerated, or are not expected to be tolerated,
  o Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

RATIONALE
The Centers for Disease Control and Prevention (CDC) Guideline for Prescribing Opioids for Chronic Pain provides recommendations for primary care clinicians who are prescribing opioids for chronic pain outside of active cancer treatment, palliative care, and end-of-life care. However, opioid immediate-release (IR) combination products include non-opioid components (acetaminophen, aspirin, and ibuprofen) with established maximum Food and Drug Administration (FDA)-labeled daily doses. FDA-labeled dosing allows for up to a maximum 24-hour dose of 4 grams (4000 mg) of acetaminophen, a maximum 24-hour dose of 4 grams (4000 mg) of aspirin, and a maximum 24-hour dose of 3200 mg of ibuprofen. Limits will apply to all patients regardless of concomitant conditions (e.g., active cancer treatment, palliative care, and end-of-life care) due to the non-opioid components.

The CDC Guideline for Prescribing Opioids for Chronic Pain recommends that when opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when increasing dosage to ≥50 morphine milligram equivalents per day (MME/day), and should avoid increasing the dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day. The immediate-release opioid combination products initial quantity limits are set for a
monthly quantity that does not exceed the maximum daily dose listed in labeling. Monthly quantities also correspond to ≤ 90 MME/day and contain ≤ 4 g/day acetaminophen or aspirin and ≤ 3200 mg/day ibuprofen. If the patient is requesting more than the initial quantity limit, then the claim will reject with a message indicating that quantity limits are exceeded. Quantities above the initial limit are not approved due to potential for serious adverse effects if FDA-labeled dosing is exceeded.

For the short-term (generally less than 10 days) management of acute pain, the recommended dose of all strengths of hydrocodone bitartrate/ibuprofen is one tablet every four to six hours as necessary. Dosages should not exceed five tablets in a 24-hour period. Since hydrocodone bitartrate/ibuprofen is only indicated for short-term use, the 1 month and 3 months limits are the same and allow for a quantity sufficient for a 10-day supply (50 tablets).

For the management of acute to moderate pain severe enough to require an opioid analgesic, the recommended dose of oxycodone and ibuprofen is one tablet every 6 hours as needed for pain. Dosage should not exceed 4 tablets in a 24-hour period and should not exceed 7 days. Since oxycodone/ibuprofen is only indicated for short-term use, the 1 month and 3 months limits are the same and allow for a quantity sufficient for a 7-day supply (28 tablets).

For the short-term (five days or less) management of acute pain, the recommended dose of Ultracet (tramadol/acetaminophen) is 2 tablets every 4 to 6 hours as needed for pain relief, up to a maximum of 8 tablets per day. Since Ultracet is only indicated for short-term use, the 1 month and 3 months limits are the same and allow for a quantity sufficient for a 5-day supply (40 tablets).

For the short-term (no more than 14 days) management of acute pain, the recommended dose of Apadaz (benzhydrocodone/acetaminophen) is 1 to 2 tablets every 4 to 6 hours as needed for pain. Dosage should not exceed 12 tablets in a 24-hour period. Since Apadaz is only indicated for short-term use, the 1 month and 3 months limits are the same and allow for a quantity sufficient for a 14-day supply (168 tablets).

**PROGRAM DESCRIPTION**

Coverage is provided without prior authorization for a 30-day or 90-day supply of an immediate-release combination product opioid for a monthly quantity that does not exceed the maximum daily dose listed in product labeling. Quantities also do not exceed 90 MME/day, 4 g/day of acetaminophen or aspirin, or 3200 mg/day of ibuprofen. Due to safety concerns for quantities that exceed FDA-labeled dosing recommendations, post limit consideration will not be given.

If the patient is requesting more than the initial quantity limit, then the claim will reject with a message indicating that quantity limits are exceeded.

**REFERENCES**


Written by: UM Development (JG)
Date Written: 04/2002

**Opioid Analgesics IR Combo Products Quantity Limits Chart**

Coverage is provided without prior authorization for a 30-day or 90-day supply of an immediate-release combination product opioid for a monthly quantity that does not exceed the maximum daily dose listed in product labeling. Quantities also do not exceed 90 MME/day (unless maximum FDA-labeled strength/dose/frequency exceeds 90 MME/day), 4 g/day of acetaminophen or aspirin, or 3200 mg/day of ibuprofen. If the patient is requesting more than the initial quantity limit, then the claim will reject with a message indicating that quantity limits are exceeded.

This quantity limit will accumulate drugs in the following 4 groups up to highest quantity listed in each group depending on the order the claims are processed: 1) Acetaminophen-containing solutions, suspensions, elixirs accumulate together, 2) Acetaminophen-containing tablets and capsules accumulate together, 2a) Acetaminophen-containing tablets with the same 1 month and 3 month limit accumulate together, 3) Aspirin-containing tablets and capsules accumulate together, 4) Ibuprofen-containing tablets accumulate together.
See Accumulation Group column in chart below for more detail.

<table>
<thead>
<tr>
<th>Accumulation Group</th>
<th>Drug/Strength</th>
<th>Labeled Dosing</th>
<th>Initial 1 Month Limit*</th>
<th>Initial 3 Month Limit*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>≤ 90 MME/day** and ≤ 4 g APAP or ASA and ≤ 3200 mg IBU (per 25 days)</td>
<td>≤ 90 MME/day** and ≤ 4 g APAP or ASA and ≤ 3200 mg IBU (per 75 days)</td>
</tr>
<tr>
<td>1</td>
<td>APAP/codeine soln 120-12 mg/5 mL</td>
<td>15 mL q4h, MAX 360 mg codeine/day</td>
<td>2700 mL (32.4 MME/day)</td>
<td>8100 mL (32.4 MME/day)</td>
</tr>
<tr>
<td>1</td>
<td>APAP/codeine susp 120-12 mg/5 mL</td>
<td>15 mL q4h, MAX 360 mg codeine/day</td>
<td>2700 mL (32.4 MME/day)</td>
<td>8100 mL (32.4 MME/day)</td>
</tr>
<tr>
<td>2</td>
<td>APAP/codeine tab 300/15 mg</td>
<td>15-60 mg codeine q4h, MAX 360 mg codeine/day</td>
<td>400 tabs (30 MME/day)</td>
<td>1200 tabs (30 MME/day)</td>
</tr>
<tr>
<td>2</td>
<td>APAP/codeine tab 300/30 mg</td>
<td>15-60 mg codeine q4h, MAX 360 mg codeine/day</td>
<td>360 tabs (54 MME/day)</td>
<td>1080 tabs (54 MME/day)</td>
</tr>
<tr>
<td>2</td>
<td>APAP/codeine tab 300/60 mg</td>
<td>15-60 mg codeine q4h, MAX 360 mg codeine/day</td>
<td>180 tabs (54 MME/day)</td>
<td>540 tabs (54 MME/day)</td>
</tr>
<tr>
<td>2</td>
<td>APAP/caffeine/dihydrocodeine cap 320.5/30/16 mg</td>
<td>2 caps q4h, MAX 10 caps/day</td>
<td>300 caps (40 MME/day)</td>
<td>900 caps (40 MME/day)</td>
</tr>
<tr>
<td>2</td>
<td>APAP/caffeine/dihydrocodeine tab 325/30/16 mg</td>
<td>2 tabs q4h, MAX 10 tabs/day</td>
<td>300 tabs (40 MME/day)</td>
<td>900 tabs (40 MME/day)</td>
</tr>
<tr>
<td>3</td>
<td>ASA/caffeine/dihydrocodeine cap 356.4/30/16 mg</td>
<td>2 caps q4h, MAX 10 caps/day</td>
<td>300 caps (40 MME/day)</td>
<td>900 caps (40 MME/day)</td>
</tr>
<tr>
<td>2</td>
<td>Benzhydrocodone/APAP 4.08 mg/325 mg</td>
<td>1-2 tabs q4-6h, MAX 12 tabs/day</td>
<td>168 tabs (60 MME/day)</td>
<td>168 tabs (60 MME/day)</td>
</tr>
<tr>
<td>2</td>
<td>Benzhydrocodone/APAP 6.12 mg/325 mg</td>
<td>1-2 tabs q4-6h, MAX 12 tabs/day</td>
<td>168 tabs (90 MME/day)</td>
<td>168 tabs (90 MME/day)</td>
</tr>
<tr>
<td>2</td>
<td>Benzhydrocodone/APAP 8.16 mg/325 mg</td>
<td>1-2 tabs q4-6h, MAX 12 tabs/day</td>
<td>168 tabs (120 MME/day)</td>
<td>168 tabs (120 MME/day)</td>
</tr>
<tr>
<td>2</td>
<td>Hydrocodone/APAP tab 2.5/325 mg</td>
<td>1-2 tabs q 4-6h, MAX 12 tabs/day</td>
<td>360 tabs (30 MME/day)</td>
<td>1080 tabs (30 MME/day)</td>
</tr>
<tr>
<td>2</td>
<td>Hydrocodone/APAP tab 5/300 mg</td>
<td>1-2 tabs q 4-6h, MAX 8 tabs/day</td>
<td>240 tabs (40 MME/day)</td>
<td>720 tabs (40 MME/day)</td>
</tr>
<tr>
<td>2</td>
<td>Hydrocodone/APAP tab 5/325 mg</td>
<td>1-2 tabs q 4-6h, MAX 8 tabs/day</td>
<td>240 tabs (40 MME/day)</td>
<td>720 tabs (40 MME/day)</td>
</tr>
<tr>
<td>2</td>
<td>Hydrocodone/APAP tab 7.5/300 mg</td>
<td>1 tab q4-6h, MAX 6 tabs/day</td>
<td>180 tabs (45 MME/day)</td>
<td>540 tabs (45 MME/day)</td>
</tr>
<tr>
<td>2</td>
<td>Hydrocodone/APAP tab 7.5/325 mg</td>
<td>1 tab q4-6h, MAX 6 tabs/day</td>
<td>180 tabs (45 MME/day)</td>
<td>540 tabs (45 MME/day)</td>
</tr>
<tr>
<td>2</td>
<td>Hydrocodone/APAP tab 10/300 mg</td>
<td>1 tab q4-6h, MAX 6 tabs/day</td>
<td>180 tabs (60 MME/day)</td>
<td>540 tabs (60 MME/day)</td>
</tr>
<tr>
<td>2</td>
<td>Hydrocodone/APAP tab 10/325 mg</td>
<td>1 tab q4-6h, MAX 6 tabs/day</td>
<td>180 tabs (60 MME/day)</td>
<td>540 tabs (60 MME/day)</td>
</tr>
<tr>
<td>1</td>
<td>Hydrocodone/APAP soln 7.5-325 mg/15 mL (5-217 mg/10 mL)</td>
<td>15 mL q4-6h, MAX 90 mL/day</td>
<td>2700 mL (45 MME/day)</td>
<td>8100 mL (45 MME/day)</td>
</tr>
<tr>
<td>1</td>
<td>Hydrocodone/APAP elixir</td>
<td>11.25 mL q4-6h, MAX 67.5 mL/day</td>
<td>2025 mL</td>
<td>6075 mL</td>
</tr>
<tr>
<td></td>
<td>Opioid/Adj Product</td>
<td>Formulation/Medication</td>
<td>Dosage/Pills/Day</td>
<td>MME Limit (Day)</td>
</tr>
<tr>
<td>---</td>
<td>--------------------------------------</td>
<td>-------------------------</td>
<td>-----------------</td>
<td>-----------------</td>
</tr>
<tr>
<td>1</td>
<td>Hydrocodone/APAP soln 10-325 mg/15 mL</td>
<td>15 mL q4-6h, MAX 90 mL/day</td>
<td>2700 mL (60 MME/day)</td>
<td>8100 mL (60 MME/day)</td>
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<tr>
<td>4</td>
<td>Hydrocodone/ibuprofen tab 2.5/200 mg</td>
<td>1 tab q4-6h, MAX 5 tabs/day</td>
<td>50 tabs (12.5 MME/day)</td>
<td>50 tabs (12.5 MME/day)</td>
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<tr>
<td>4</td>
<td>Hydrocodone/ibuprofen tab 5/200 mg</td>
<td>1 tab q4-6h, MAX 5 tabs/day</td>
<td>50 tabs (25 MME/day)</td>
<td>50 tabs (25 MME/day)</td>
</tr>
<tr>
<td>4</td>
<td>Hydrocodone/ibuprofen tab 7.5/200 mg</td>
<td>1 tab q4-6h, MAX 5 tabs/day</td>
<td>50 tabs (37.5 MME/day)</td>
<td>50 tabs (37.5 MME/day)</td>
</tr>
<tr>
<td>1</td>
<td>Oxycodone/APAP soln 5/325 mg/5 mL</td>
<td>5 mL q6h, MAX 60 mL/day</td>
<td>1800 mL (90 MME/day)</td>
<td>5400 mL (90 MME/day)</td>
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<tr>
<td>2</td>
<td>Oxycodone/APAP tab 2.5/300 mg</td>
<td>1-2 tabs q6h, MAX 12 tabs/day</td>
<td>360 tabs (45 MME/day)</td>
<td>1080 tabs (45 MME/day)</td>
</tr>
<tr>
<td>2</td>
<td>Oxycodone/APAP tab 2.5/325 mg</td>
<td>1-2 tabs q6h, MAX 12 tabs/day</td>
<td>360 tabs (45 MME/day)</td>
<td>1080 tabs (45 MME/day)</td>
</tr>
<tr>
<td>2</td>
<td>Oxycodone/APAP tab 5/300 mg</td>
<td>1 tab q6h, MAX 12 tabs/day</td>
<td>360 tabs (90 MME/day)</td>
<td>1080 tabs (90 MME/day)</td>
</tr>
<tr>
<td>2</td>
<td>Oxycodone/APAP tab 5/325 mg</td>
<td>1 tab q6h, MAX 12 tabs/day</td>
<td>360 tabs (90 MME/day)</td>
<td>1080 tabs (90 MME/day)</td>
</tr>
<tr>
<td>2</td>
<td>Oxycodone/APAP tab 7.5/300 mg</td>
<td>1 cap q6h, MAX 8 tabs/day</td>
<td>240 tabs (90 MME/day)</td>
<td>720 tabs (90 MME/day)</td>
</tr>
<tr>
<td>2</td>
<td>Oxycodone/APAP tab 7.5/325 mg</td>
<td>1 tab q6h, MAX 8 tabs/day</td>
<td>240 tabs (90 MME/day)</td>
<td>720 tabs (90 MME/day)</td>
</tr>
<tr>
<td>2</td>
<td>Oxycodone/APAP tab 10/300 mg</td>
<td>1 tab q6h, MAX 6 tabs/day</td>
<td>180 tabs (90 MME/day)</td>
<td>540 tabs (90 MME/day)</td>
</tr>
<tr>
<td>2</td>
<td>Oxycodone/APAP tab 10/325 mg</td>
<td>1 tab q6h, MAX 6 tabs/day</td>
<td>180 tabs (90 MME/day)</td>
<td>540 tabs (90 MME/day)</td>
</tr>
<tr>
<td>3</td>
<td>Oxycodone/ASA tab 4.8355/325 mg</td>
<td>1 tab q6h, MAX 12 tabs/day</td>
<td>360 tabs (87 MME/day)</td>
<td>1080 tabs (87 MME/day)</td>
</tr>
<tr>
<td>4</td>
<td>Oxycodone/ibuprofen tab 5/400 mg</td>
<td>1 tab q6h, MAX 4 tabs/day</td>
<td>28 tabs (30 MME/day)</td>
<td>28 tabs (30 MME/day)</td>
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<tr>
<td>2a</td>
<td>Tramadol/APAP 37.5/325 mg</td>
<td>2 tabs q4-6h, MAX 8 tabs/day</td>
<td>40 tabs (30 MME/day)</td>
<td>40 tabs (30 MME/day)</td>
</tr>
</tbody>
</table>

*The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing. Limits are set up as quantity versus time edits.

**Unless maximum FDA-labeled strength/dose/frequency exceeds 90 MME/day.
SPECIALTY GUIDELINE MANAGEMENT

Opsumit (macitentan)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Opsumit is an endothelin receptor antagonist (ERA) indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) to delay disease progression. Disease progression included: death, initiation of intravenous or subcutaneous prostanoids, or clinical worsening of PAH (decreased 6-minute walk distance, worsened PAH symptoms and need for additional PAH treatment). Opsumit also reduced hospitalization for PAH.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Pulmonary Arterial Hypertension (PAH)
Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:
A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
B. PAH was confirmed by either criterion (1) or criterion (2) below:
   1. Pretreatment right heart catheterization with all of the following results:
      i.  mPAP ≥ 25 mmHg
      ii. PCWP ≤ 15 mmHg
      iii. PVR > 3 Wood units
   2. For infants less than one year of age with any of the following conditions, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed:
      i. Post cardiac surgery
      ii. Chronic heart disease
      iii. Chronic lung disease associated with prematurity
      iv. Congenital diaphragmatic hernia

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section II who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. APPENDIX
WHO Classification of Pulmonary Hypertension

1 PAH
1.1 Idiopathic (PAH)
1.2 Heritable PAH
1.3 Drug- and toxin-induced PAH
1.4. PAH associated with:
   1.4.1 Connective tissue diseases
   1.4.2 HIV infection
   1.4.3 Portal hypertension
   1.4.4 Congenital heart diseases
   1.4.5 Schistosomiasis
1.5 PAH long-term responders to calcium channel blockers
1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease
2.1 PH due to heart failure with preserved LVEF
2.2 PH due to heart failure with reduced LVEF
2.3 Valvular heart disease
2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia
3.1 Obstructive lung disease
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction
4.1 Chronic thromboembolic PH
4.2 Other pulmonary artery obstructions
   4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
   4.2.2 Other malignant tumors
   Renal carcinoma
   Uterine carcinoma
   Germ cell tumours of the testis
   Other tumours
   4.2.3 Non-malignant tumours
   Uterine leiomyoma
   4.2.4 Arteritis without connective tissue disease
   4.2.5 Congenital pulmonary artery stenosis
   4.2.6 Parasites
   Hydatidosis

5 PH with unclear and/or multifactorial mechanisms
5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
5.4 Complex congenital heart disease
V. REFERENCES

## PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>ORAL/INTRANASAL FENTANYL PRODUCTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRAND NAME* (generic)</td>
<td></td>
</tr>
<tr>
<td>ABSTRAL</td>
<td>(fentanyl citrate sublingual tablet)</td>
</tr>
<tr>
<td>ACTIQ</td>
<td>(fentanyl citrate oral transmucosal lozenge)</td>
</tr>
<tr>
<td>FENTORA</td>
<td>(fentanyl citrate buccal tablet)</td>
</tr>
<tr>
<td>LAZANDA</td>
<td>(fentanyl nasal spray)</td>
</tr>
<tr>
<td>ONSOLIS</td>
<td>(fentanyl buccal soluble film)</td>
</tr>
<tr>
<td>SUBSYS</td>
<td>(fentanyl sublingual spray)</td>
</tr>
</tbody>
</table>

**Status:** CVS Caremark Criteria  
**Type:** Initial Prior Authorization  
**Ref # 288-C**

*Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

### FDA-APPROVED INDICATIONS

**Abstral**  
Abstral (fentanyl citrate sublingual tablet) is indicated for the management of breakthrough pain in cancer patients 18 years of age and older who are already receiving and who are tolerant to, around-the-clock opioid therapy for their underlying persistent cancer pain.

**Actiq**  
Actiq (fentanyl citrate oral transmucosal lozenge) is indicated for the management of breakthrough pain in cancer patients 16 years of age and older who are already receiving and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain.

**Fentora**  
Fentora (fentanyl citrate buccal tablet) is indicated for the management of breakthrough pain in cancer patients 18 years of age and older who are already receiving and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain.
Lazanda
Lazanda (fentanyl nasal spray) is indicated for the management of breakthrough pain in cancer patients 18 years of age and older who are already receiving and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain.

Onsolis
Onsolis (fentanyl buccal soluble film) is indicated for the management of breakthrough pain in cancer patients 18 years of age and older who are already receiving and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain.

Subsys
Subsys (fentanyl sublingual spray) is indicated for the management of breakthrough pain in cancer patients 18 years of age and older who are already receiving and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain.

For All Oral/Intranasal Fentanyl Products:
Patients considered opioid tolerant are those who are taking around-the-clock medicine consisting of at least 60 mg of oral morphine per day, at least 25 mcg per hour of transdermal fentanyl, at least 30 mg of oral oxycodone per day, at least 60 mg of oral hydrocodone per day, at least 8 mg of oral hydromorphone per day, at least 25 mg of oral oxymorphone per day, or an equianalgesic dose of another opioid medication daily for one week or longer. Patients must remain on around-the-clock opioids when taking the requested oral/intranasal fentanyl product.

Limitations of Use:
- Not for use in opioid non-tolerant patients.
- Not for use in the management of acute or postoperative pain, including headache/migraine, dental pain, or in the emergency department.
- As a part of the TIRF REMS Access program, oral/intranasal fentanyl products may be dispensed only to outpatients enrolled in the program. For inpatient administration of oral/intranasal fentanyl products (e.g., hospitals, hospices, and long-term care facilities that prescribe for inpatient use), patient and prescriber enrollment is not required.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:
- The requested drug is indicated for the treatment of breakthrough CANCER-related pain only. The requested drug is being prescribed for the management of breakthrough pain in a CANCER patient who is currently receiving around-the-clock opioid therapy for underlying CANCER pain. The prescriber must submit chart notes or other documentation supporting a diagnosis of cancer-related pain and list the type of cancer. [Note: For drug coverage approval, ICD diagnosis code provided MUST support the CANCER-RELATED DIAGNÓSIS.]
  AND
- Chart notes or other documentation supporting a diagnosis of cancer-related pain have been submitted to CVS Health
  AND
- If additional quantities are being requested, then:
  - The patient’s dose of a concomitant long-acting analgesic is being increased
  OR
  - Additional quantities of the requested drug are needed for breakthrough pain because the dose of the patient’s long-acting analgesic is unable to be increased
[Note: Ensure that the patient can safely take the requested dose based on their history of opioid use.]

Quantity Limits apply.
RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Abstral, Actiq, Fentora, Lazanda, Onsolis, and Subsys are indicated for the management of breakthrough pain in cancer patients who are already receiving and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain. Patients considered opioid tolerant are those who are taking, for one week or longer, around-the-clock medicine consisting of at least 60 mg of oral morphine per day, at least 25 mcg per hour of transdermal fentanyl, at least 30 mg of oral oxycodone per day, at least 60 mg of oral hydrocodone per day, at least 8 mg of oral hydromorphone per day, at least 25 mg of oral oxymorphone per day, or an equianalgesic dose of another opioid medication daily for one week or longer. Patients must remain on around-the-clock opioids when taking the requested oral/intranasal fentanyl product. Oral/intranasal fentanyl products are not for use in opioid non-tolerant patients. Oral/intranasal fentanyl products are not for use in the management of acute or postoperative pain, including headache/migraine, dental pain, or in the emergency department. As a part of the Transdermal Immediate-Release Fentanyl (TIRF) Risk Evaluation and Mitigation Strategies (REMS) Access program, oral/intranasal fentanyl products may be dispensed only to outpatients enrolled in the program. For inpatient administration of oral/intranasal fentanyl products (e.g., hospitals, hospices, and long-term care facilities that prescribe for inpatient use), patient and prescriber enrollment is not required.1-8

For patients who are tolerant to and currently receiving opioid therapy for persistent cancer pain, dosing should be individually titrated to provide adequate analgesia with minimal side effects. Oral/intranasal fentanyl products should be limited to four or fewer doses per day. When the breakthrough pain episode is not relieved after administration of one dose, an additional dose may be necessary. If the patient requires more than 1 dose per breakthrough pain episode for several consecutive episodes, dose titration may be necessary. Patients experiencing >4 breakthrough pain episodes/day should have the dose of their long-term opioid re-evaluated.1-8 Prescribers should ensure that the patient can safely take the requested dose based on their history of opioid use.

Based on this information, a limit of four units per day, or 120 units per month, will be placed on Abstral, Actiq, Fentora, Onsolis, and Subsys 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg. A limit of 240 sprays per month (i.e., 120 blisters per month) will be placed on Subsys 1200 mcg and 1600 mcg since two sprays of 600 mcg are needed to achieve the 1200 mcg dose and two sprays of 800 mcg are needed to achieve the 1600 mcg dose. A limit of 30 bottles per month will be placed on the Lazanda products since each bottle provides 8 sprays.

For patients undergoing dose titration (increase) of their concomitant long-acting analgesic or in situations where it is not clinically appropriate to increase the dose of the long-acting analgesic, an additional quantity may be available. This additional quantity will provide coverage for an amount sufficient for up to 4 episodes of breakthrough pain per day plus two additional doses per day. A limit of 6 units per day, or 180 units per month, will be placed on Abstral 100 mcg, 200 mcg, 300 mcg, 400 mcg, Actiq (all strengths), Fentora (all strengths), Onsolis 200 mcg, 400 mcg, 600 mcg, and Subsys 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg. For Subsys 1200 mcg and 1600 mcg, a higher limit of 12 sprays per day (i.e., 6 blisters), or 360 sprays per month (i.e., 180 blisters), will be in place. For Lazanda 100 mcg, a higher limit of 12 sprays per day, or 45 bottles per month, will be in place.

Coverage for Abstral 600 mcg or 800 mcg, Lazanda 300 mcg or 400 mcg, Onsolis 800 mcg or 1200 mcg is only provided for up to 4 units (Abstral, Onsolis) or 8 sprays (Lazanda) per day to avoid exceeding the labeled maximum dose.

REFERENCES


Written by: UM Development (JG)
Date Written: 04/2002
Revised:
(MB) 08/2004; (NB) 08/2005; (CT) 08/2006; (NB) 11/2006 (Added Fentora); (RP) 03/2007 (update label); (CT) 07/2007; (AM) 08/2008; (SE) 08/2009; (RB/AH/SE) 06/2010; (SE) 01/2011 (Added Abstral; Clarified age restriction question), 08/2011, 01/2012 added Subsys (08-2011 (2)), 03/2012, 03/2013, 07/2013 (changed to commercial reference number); (SE/MT) 01/2014; (SE) 06/2014, 01/2015; (CF) 08/2015 (Added Onsolis, additional cancer question, documentation/tech notes), 10/2015 (added questions for additional quantities), 01/2016 (added Lazanda questions for macro compatibility, no clinical changes), 06/2016 (new strength of Lazanda – 300 mcg); 12/2016 (updated denial reasons, no clinical changes); (JH/CF) 01/2017, 07/2017 (clarified qty for Subsys 1200 mcg and 1600 mcg), 01/2018, 08/2018 (added note); (CF/DS) 01/2019 (no clinical changes)

Reviewed:
Medical Affairs: 04/2002; (MM) 08/2004, 08/2005, 08/2006; (WF) MD 07/2007, 08/2008, 08/2009; (KP) 06/2010, 01/2011, 08/2011, 01/2012, 03/2012; (DNC) 03/2013; (LMS) 07/2013; (KP) 01/2014; (SES) 06/2014, 01/2015; (ADA) 08/2015; (DNC) 10/2015; (ME) 06/2016; (DNC) 01/2017, 07/2017, 01/2018; (MC) 06/2018

---

**CRITERIA FOR APPROVAL**

1. The requested drug is indicated for the treatment of breakthrough CANCER-related pain only. Is the requested drug being prescribed for the management of breakthrough pain in a CANCER patient who is currently receiving around-the-clock opioid therapy for underlying CANCER pain?

   If yes, then prescriber MUST submit chart notes or other documentation supporting a diagnosis of cancer-related pain AND list type of cancer__________________________

   [Note: For drug coverage approval, ICD diagnosis code provided MUST support the CANCER-RELATED DIAGNOSIS.]

2. Have chart notes or other documentation supporting a diagnosis of cancer-related pain been submitted to CVS Health?

   [Tech Note: MUST obtain a physical copy of chart notes or other documentation supporting a diagnosis of cancer-related pain AND verify that the prescriber has listed the type of cancer. If the PA is worked over the phone, then the prescriber still MUST submit physical chart notes or other documentation. If a physical copy of documentation of a diagnosis of cancer-related pain is not received, then the PA should be denied.]

3. Which drug is being requested? Please check the drug being requested.

   [Note: Ensure that the patient can safely take the requested dose based on their history of opioid use.]

   - Abstral 600 mcg or 800 mcg (if checked, then go to 4)
   - Abstral 100 mcg, 200 mcg, 300 mcg, 400 mcg (if checked, then go to 6)
   - Actiq (all strengths) (if checked, then go to 6)
   - Fentora (all strengths) (if checked, then go to 6)
   - Onsolis 200 mcg, 400 mcg, 600 mcg (if checked, then go to 6)
   - Onsolis 800 mcg or 1200 mcg (if checked, then go to 4)
   - Lazanda 100 mcg (if checked, then go to 7)
   - Lazanda 300 mcg or 400 mcg (if checked, then go to 5)
   - Subsys 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg (if checked, then go to 6)
4. Coverage is provided for up to 120 units per month of the following: A) Abstral 600 mcg, 800 mcg, B) Onsolis 800 mcg, 1200 mcg. Is MORE than this quantity needed to manage the patient’s pain? [No further questions.]

[RPh Note: If yes, then deny and enter a partial approval for up to 120 units per month of the following: A) Abstral 600 mcg, 800 mcg, B) Onsolis 800 mcg, 1200 mcg.]

5. Coverage is provided for up to 240 sprays per month (i.e., 30 bottles per month) of Lazanda 300 mcg, 400 mcg. Is MORE than this quantity needed to manage the patient’s pain? [No further questions.]

[RPh Note: If yes, then deny and enter a partial approval for 240 sprays per month (i.e., 30 bottles per month) of Lazanda 300 mcg, 400 mcg.]

6. Coverage is provided for up to 120 units per month of the following: A) Abstral 100 mcg, 200 mcg, 300 mcg, 400 mcg, B) Actiq (all strengths), C) Fentora (all strengths), D) Onsolis 200 mcg, 400 mcg, 600 mcg, E) Subsys 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg. If higher quantities are needed, then additional questions are required. Is MORE than this quantity needed to manage the patient’s pain? [Note Subsys packaging: Supplied as 1 spray per blister for Subsys 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg.] [If no, then no further questions.]

[If yes, then skip to question 9.]

7. Coverage is provided for up to 240 sprays per month (i.e., 30 bottles per month) of Lazanda 100 mcg. If higher quantities are needed, then additional questions are required. Is MORE than this quantity needed to manage the patient’s pain? [If no, then no further questions.]

[If yes, then skip to question 9.]

8. Coverage is provided for up to 240 sprays per month (i.e., 120 blisters per month) of Subsys 1200 mcg or 1600 mcg. If higher quantities are needed, then additional questions are required. Is MORE than this quantity needed to manage the patient’s pain? [Note Subsys packaging: Supplied as 2 sprays per blister for Subsys 1200 mcg and 1600 mcg.] [If no, then no further questions.]

9. Is the patient’s dose of a concomitant long-acting analgesic being increased? [If yes, then skip to question 11.]

10. Are additional quantities of the requested drug needed for breakthrough pain because the dose of the patient’s long-acting analgesic is unable to be increased? [If no, then no further questions.]

[Note: Additional questions if no, then deny and enter a partial approval for the following: A) 120 units per month of Abstral, Actiq, Fentora, Onsolis, or Subsys 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg, B) 240 sprays per month (i.e., 120 bottles per month) of Lazanda 100 mcg, C) 240 sprays per month (i.e., 120 blisters per month) of Subsys 1200 mcg or 1600 mcg.]
11 Which drug is being requested? Please check the drug being requested. 
[Note: Ensure that the patient can safely take the requested dose based on their history of opioid use.]

[ ] Abstral 100 mcg, 200 mcg, 300 mcg, 400 mcg (if checked, then go to 12)
[ ] Actiq (all strengths) (if checked, then go to 12)
[ ] Fentora (all strengths) (if checked, then go to 12)
[ ] Onsolis 200 mcg, 400 mcg, 600 mcg (if checked, then go to 12)
[ ] Lazanda 100 mcg (if checked, then go to 13)
[ ] Subsys 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg (if checked, then go to 12)
[ ] Subsys 1200 mcg, 1600 mcg (if checked, then go to 14)

12 Does the patient’s pain require use of MORE than 180 units per month of any of the following:  
A) Abstral 100 mcg, 200 mcg, 300 mcg, 400 mcg, B) Actiq (all strengths), C) Fentora (all strengths),  
D) Onsolis 200 mcg, 400 mcg, 600 mcg, E) Subsys 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg?  
[Note Subsys packaging: Supplied as 1 spray per blister for Subsys 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg.]  
[No further questions.]

[RPh Note: If yes, then deny and enter a partial approval for the following:  
A) Abstral 100 mcg, 200 mcg, 300 mcg, 400 mcg, B) Actiq (all strengths), C) Fentora (all strengths),  
D) Onsolis 200 mcg, 400 mcg, 600 mcg, E) Subsys 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg.]

13 Does the patient’s pain require use of MORE than 360 sprays per month (i.e., 45 bottles per month) of Lazanda 100 mcg?  
[No further questions.]

[Note Subsys packaging: Supplied as 2 sprays per blister for Subsys 1200 mcg and 1600 mcg.

14 Does the patient’s pain require use of MORE than 360 sprays per month (i.e., 180 blisters per month) of Subsys 1200 mcg or 1600 mcg?  
[No further questions.]

[Note Subsys packaging: Supplied as 2 sprays per blister for Subsys 1200 mcg and 1600 mcg.

1. Go to 2
2. Deny

DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
You do not meet the requirements of your plan. Your plan covers this drug when you are currently taking opioid drugs around-the-clock for cancer pain and you need to manage your breakthrough cancer pain. Your request has been denied based on the information we have.
[Short Description: No approvable diagnosis.]
<p>| | | | |</p>
<table>
<thead>
<tr>
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<th></th>
<th></th>
<th></th>
</tr>
</thead>
</table>
| 2. | Go to 3 | Deny | You do not meet the requirements of your plan. Your plan covers this drug when your prescriber submits your chart notes or other documentation that supports that you have pain due to cancer to CVS Health. Your request has been denied based on the information we have.  
[Short Description: Prescriber did not fax documentation to confirm cancer-related pain.] |
| 3. | 1=4; 2=6; 3=6; 4=6; 5=6; 6=4; 7=7; 8=5; 9=6; 10=8 | N/A |   |
| 4. | Deny | Approve, 12 months  
120 units per 25 days or 360 units per 75 days* of:  
Abstral 600 mcg, 800 mcg  
Onsolis 800 mcg, 1200 mcg | You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 120 units per month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.  
[Short Description: Over max quantity.] |
| 5. | Deny | Approve, 12 months  
30 bottles per 25 days or 90 bottles per 75 days* of:  
Lazanda 300 mcg, 400 mcg | You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 240 sprays per month (i.e., 30 bottles per month) of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.  
[Short Description: Over max quantity.] |
| 6. | Go to 9 | Approve, 12 months  
120 units per 25 days OR 360 units per 75 days* of:  
Abstral 100 mcg, 200 mcg, 300 mcg, 400 mcg  
Actiq (all strengths)  
Fentora (all strengths)  
Onsolis 200 mcg, 400 mcg, 600 mcg  
Subsys 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg |   |
| 7. | Go to 9 | Approve, 12 months  
30 bottles per 25 days or 90 bottles per 75 days* of:  
Lazanda 100 mcg |   |
<p>| 8. | Go to 9 | Approve, 12 months |   |</p>
<table>
<thead>
<tr>
<th>9.</th>
<th>Go to 11</th>
<th>Go to 10</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.</td>
<td>Go to 11</td>
<td>Deny</td>
</tr>
<tr>
<td></td>
<td>RPh Note: For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>You have requested more than the quantity allowed by your plan. Current plan approved criteria cover up to:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- 120 units per month of Abstral, Actiq, Fentora, Onsolis, or Subsys 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- 240 sprays per month (i.e., 30 bottles per month) of Lazanda</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- 240 sprays per month (i.e., 120 blisters per month) of Subsys 1200 mcg or 1600 mcg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>You have been approved for the quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Your plan covers additional quantities of this drug when you meet any of these conditions:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- The dose of your long-acting opioid drug is being increased</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- The dose of your long-acting opioid drug is unable to be increased and you need more of the requested drug to manage your breakthrough pain</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Your use of this drug does not meet the requirement. This is based on the information we have.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>[Short Description: Over max quantity and patient does not meet requirements for additional quantities.]</td>
<td></td>
</tr>
<tr>
<td>11.</td>
<td>1=12; 2=12; 3=12; 4=12; 5=13; 6=12; 7=14</td>
<td>N/A</td>
</tr>
<tr>
<td>12.</td>
<td>Deny</td>
<td>Approve, 12 months</td>
</tr>
<tr>
<td></td>
<td>180 units per 25 days OR 540 units per 75 days* of:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Abstral 100 mcg, 200 mcg, 300 mcg, 400 mcg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Actiq (all strengths)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fentora (all strengths)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Onsolis 200 mcg, 400 mcg, 600 mcg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Subsys 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 180 units/month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>[Short Description: Over max quantity.]</td>
<td></td>
</tr>
<tr>
<td>13.</td>
<td>Deny</td>
<td>Approve, 12 months</td>
</tr>
<tr>
<td></td>
<td>45 bottles per 25 days or 135 bottles per 75 days* of:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 45 bottles/month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lazanda 100 mcg</td>
<td>duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.</td>
</tr>
<tr>
<td>---</td>
<td>----------------</td>
<td>-------------------------------------------------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| 14. | Deny | Approve, 12 months  
360 sprays (i.e., 180 blisters) per 25 days or 1080 sprays (i.e., 540 blisters) per 75 days* of Subsys 1200 mcg or 1600 mcg  
You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 360 sprays (i.e., 180 blisters)/month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. |

*The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.
SPECIALTY GUIDELINE MANAGEMENT
ORENCIA (abatacept)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
1. Moderately to severely active rheumatoid arthritis in adults
2. Moderately to severely active polyarticular juvenile idiopathic arthritis in patients 2 years of age or older
3. Active psoriatic arthritis in adults

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active rheumatoid arthritis (RA)
   1. Authorization of 24 months may be granted for members who have previously received Orencia or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) indicated for the treatment of moderately to severely active rheumatoid arthritis.
   2. Authorization of 24 months may be granted for treatment of moderately to severely active RA when any of the following criteria is met:
      a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
      b. Member has an intolerance or contraindication to methotrexate (see Appendix).

B. Moderately to severely active polyarticular juvenile idiopathic arthritis (pJIA)
   1. Authorization of 24 months may be granted for members who have previously received Orencia or Actemra.
   2. Authorization of 24 months may be granted for treatment of active pJIA when any of the following criteria is met:
      a. Member has experienced an inadequate response to at least a 3-month trial of a TNF inhibitor.
      b. Member has intolerance or contraindication to a TNF inhibitor.

C. Active psoriatic arthritis (PsA)
   Authorization of 24 months may be granted for treatment of active psoriatic arthritis (PsA).
III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Orencia as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB).

Note: Members who have received Orencia or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) are exempt from requirements related to TB screening in this Policy.

V. APPENDIX: Examples of Contraindications to Methotrexate

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodyplasia
9. Pregnancy or planning pregnancy (male or female)
10. Renal impairment
11. Significant drug interaction

VI. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

Orenitram
(treprostinil extended-release tablets)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Orenitram is indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise capacity.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:
A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
B. PAH was confirmed by either criterion (1) or criterion (2) below:
   1. Pretreatment right heart catheterization with all of the following results:
      i. mPAP ≥ 25 mmHg
      ii. PCWP ≤ 15 mmHg
      iii. PVR > 3 Wood units
   2. For infants less than one year of age with any of the following conditions, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed:
      i. Post cardiac surgery
      ii. Chronic heart disease
      iii. Chronic lung disease associated with prematurity
      iv. Congenital diaphragmatic hernia

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section II who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. APPENDIX

WHO Classification of Pulmonary Hypertension
1 PAH
1.1 Idiopathic (PAH)
1.2 Heritable PAH
1.3 Drug- and toxin-induced PAH
1.4. PAH associated with:
   1.4.1 Connective tissue diseases
   1.4.2 HIV infection
   1.4.3 Portal hypertension
   1.4.4 Congenital heart diseases
   1.4.5 Schistosomiasis
1.5 PAH long-term responders to calcium channel blockers
1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease
2.1 PH due to heart failure with preserved LVEF
2.2 PH due to heart failure with reduced LVEF
2.3 Valvular heart disease
2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia
3.1 Obstructive lung disease
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction
4.1 Chronic thromboembolic PH
4.2 Other pulmonary artery obstructions
   4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
   4.2.2 Other malignant tumors
      Renal carcinoma
      Uterine carcinoma
      Germ cell tumours of the testis
      Other tumours
   4.2.3 Non-malignant tumours
      Uterine leiomyoma
   4.2.4 Arteritis without connective tissue disease
   4.2.5 Congenital pulmonary artery stenosis
   4.2.6 Parasites
      Hydatidosis

5 PH with unclear and/or multifactorial mechanisms
5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
5.4 Complex congenital heart disease

V. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

ORFADIN (nitisinone)
NITYR (nitisinone)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Orfadin is indicated for the treatment of adult and pediatric patients with hereditary tyrosinemia type 1 (HT-1) in combination with dietary restriction of tyrosine and phenylalanine.

Nityr is indicated for the treatment of patients with hereditary tyrosinemia type 1 (HT-1) in combination with dietary restriction of tyrosine and phenylalanine.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of indefinite approval may be granted for treatment of hereditary tyrosinemia type 1 (HT-1) when the diagnosis is confirmed by biochemical testing (e.g., detection of succinylacetone in urine) or DNA testing (mutation analysis).

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCE

PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>BRAND NAME* (generic)</th>
<th>ORILISSA (elagolix)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Status: CVS Caremark Criteria</td>
<td>Type: Initial Prior Authorization</td>
</tr>
<tr>
<td>Ref # 2634-A</td>
<td></td>
</tr>
</tbody>
</table>

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS
Orilissa is indicated for the management of moderate to severe pain associated with endometriosis.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has the diagnosis of moderate to severe pain associated with endometriosis
  AND
- The patient has not received the maximum recommended treatment course of 12 months of Lupron Depot or Lupaneta Pack or 6 months of Synarel or Zoladex
  AND
  - The patient will receive 150 mg once daily of the requested drug
  AND
  - The patient has not already received greater than or equal to 24 months of therapy of the requested drug
  OR
  - The patient will receive 200 mg twice daily of the requested drug
  AND
  - The patient has not already received greater than or equal to 6 months of therapy of the requested drug

RATIONALE
The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Orilissa is indicated for the management of moderate to severe pain associated with endometriosis.3, 6-7

Nonsteroidal anti-inflammatory drugs (NSAIDs) are often the first-line treatment for endometriosis, followed by hormone therapy. If NSAIDs and hormonal contraceptives are ineffective, then the next step is treatment with a gonadotropin-releasing hormone (GnRH) analogue such as leuprolide, goserelin (Zoladex)8, or nafarelin (Synarel). GnRH analogues may have significant side effects, including hot flushes, vaginal dryness, and osteopenia. Osteopenia has been shown to be reversible with short-term use, but may not be with long-term use or use of multiple cycles.9 Due to risk of osteopenia and bone loss, Orilissa will not be approved if the patient has received a 12-month1-2 treatment course of Lupron Depot or Lupaneta Pack or a 6-month4-5 course of Zoladex or Synarel.

Danazol, an androgen, is effective in the treatment of pelvic pain associated with endometriosis. However, androgenic adverse effects, such as acne, hirsutism, and male pattern baldness often limit its use. The drug has several United States Food and Drug Administration boxed warnings, including the risk of thrombosis and teratogenicity.8 Due to significant adverse effects, a trial of Danazol is not required.

Orilissa causes a dose-dependent decrease in bone mineral density (BMD). BMD loss is greater with increasing duration of use and may not be completely reversible after stopping treatment. It is recommended to limit the duration of use to reduce the extent of bone loss. The use of higher doses increases exposures and risk for bone loss.3, 6-7 Therefore, the duration of approval is 24 months for patients taking a maximum of 150 mg once daily, and the duration of approval is 6 months for patients taking 200 mg twice daily.
REFERENCES

Written by: UM Development (DS/AH/NP)
Date Written: 08/2018
Revised: (CF) 12/2018 (no clinical changes)
Reviewed: Medical Affairs: (ME) 08/2018
External Review: 10/2018, 04/2019

CRITERIA FOR APPROVAL

1. Does the patient have the diagnosis of moderate to severe pain associated with endometriosis? Yes No
2. Has the patient received the maximum recommended treatment course of 12 months of Lupron Depot or Lupaneta Pack OR 6 months of Synarel or Zoladex? Yes No
3. Will the patient receive 150 mg once daily of the requested drug? [If no, then skip to question 5.] Yes No
4. Has the patient already received greater than or equal to 24 months of therapy of the requested drug? [No further questions.] Yes No
5. Will the patient receive 200 mg twice daily of the requested drug? Yes No
6. Has the patient already received greater than or equal to 6 months of therapy of the requested drug? Yes No
<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
<th>DENIAL REASONS – DO NOT USE FOR MEDICARE PART D</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Go to 2</td>
<td>Deny</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have moderate to severe pain associated with endometriosis. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis.]</td>
</tr>
<tr>
<td>2.</td>
<td>Deny</td>
<td>Go to 3</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have not taken full treatment courses of any of the following: - Lupron Depot for 12 months - Lupaneta Pack for 12 months - Synarel for 6 months - Zoladex for 6 months Your request has been denied based on the information we have. [Short Description: Prior therapy exclusion.]</td>
</tr>
<tr>
<td>3.</td>
<td>Go to 4</td>
<td>Go to 5</td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>Deny</td>
<td>Approve, 24 months</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when the prescribed dose and duration falls within the manufacturer’s published dosing guidelines. Your request has been denied based on the information we have. [Short Description: Unapproved dose and/or duration.]</td>
</tr>
<tr>
<td>5.</td>
<td>Go to 6</td>
<td>Deny</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when the prescribed dose falls within the manufacturer’s published dosing guidelines. Your request has been denied based on the information we have. [Short Description: Unapproved dose.]</td>
</tr>
<tr>
<td>6.</td>
<td>Deny</td>
<td>Approve, 6 months</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when the prescribed dose and duration falls within the manufacturer’s published dosing guidelines. Your request has been denied based on the information we have. [Short Description: Unapproved dose and/or duration.]</td>
</tr>
</tbody>
</table>
SPECIALTY GUIDELINE MANAGEMENT

ORKAMBI (lumacaftor/ivacaftor)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Orkambi is indicated for the treatment of cystic fibrosis (CF) in patients age 2 years and older who are homozygous for the F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. If the patient’s genotype is unknown, an FDA cleared CF mutation test should be used to detect the presence of the F508del mutation on both alleles of the CFTR gene.

Limitation of use: The efficacy and safety of Orkambi have not been established in patients with CF other than those homozygous for the F508del mutation.

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review: genetic testing report confirming the presence of the appropriate CFTR gene mutation.

III. CRITERIA FOR INITIAL APPROVAL

Cystic Fibrosis

Indefinite authorization may be granted for treatment of cystic fibrosis when all of the following criteria are met:

A. Genetic testing was conducted to detect a mutation in the CFTR gene.
B. The member is positive for the F508del mutation on both alleles of the CFTR gene.
C. The member is at least 2 years of age.
D. Orkambi will not be used in combination with Kalydeco or Symdeko.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

OTEZLA (apremilast)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Moderate to severe plaque psoriasis
   2. Active psoriatic arthritis
   3. Oral ulcers associated with Behçet’s disease

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderate to severe plaque psoriasis
   1. Authorization of 24 months may be granted for members who have previously received Otezla or any biologic disease-modifying antirheumatic drug (DMARD) indicated for the treatment of moderate to severe plaque psoriasis.

   2. Authorization of 24 months may be granted for treatment of moderate to severe plaque psoriasis when all of the following criteria are met:
      a. At least 5% of BSA is affected OR crucial body areas (i.e., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
      b. Member meets any of the following criteria:
         i. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
         ii. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine or acitretin (see Appendix A).

B. Active psoriatic arthritis (PsA)
   Authorization of 24 months may be granted for treatment of active psoriatic arthritis (PsA).

C. Behcet’s syndrome
   Authorization of 24 months may be granted for members who have previously received Otezla or any biologic indicated for the treatment of Behcet’s syndrome.

   Authorization of 24 months may be granted for the treatment of oral ulcers associated with Behçet’s syndrome when the member has had an inadequate response to at least one nonbiologic medication for Behçet’s disease (e.g., colchicine, systemic glucocorticoids, azathioprine).
III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 4 months of therapy with Otezla as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. Appendix A: Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin.

1. Alcoholism, alcoholic liver disease, or other chronic liver disease
2. Breastfeeding
3. Drug interaction
4. Cannot be used due to risk of treatment-related toxicity
5. Pregnancy or planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

OTREXUP (methotrexate injection)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
1. Rheumatoid Arthritis (RA) including Polyarticular Juvenile Idiopathic Arthritis (pJIA)
   Otrexup is indicated in the management of selected adults with severe, active rheumatoid arthritis (RA) or children with active polyarticular juvenile idiopathic arthritis (pJIA), who have had an insufficient therapeutic response to, or are intolerant of, an adequate trial of first-line therapy including full dose non-steroidal anti-inflammatory agents (NSAIDs).
2. Psoriasis
   Otrexup is indicated in adults for the symptomatic control of severe, recalcitrant, disabling psoriasis that is not adequately responsive to other forms of therapy, but only when the diagnosis has been established, as by biopsy and/or after dermatologic consultation. It is important to ensure that a psoriasis “flare” is not due to an undiagnosed concomitant disease affecting immune responses.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 24 months may be granted for treatment of RA, pJIA, or psoriasis when BOTH of the following criteria are met:
A. Member has tried and had an inadequate response or intolerance to generic oral methotrexate.
B. Member has inability to prepare and administer generic injectable methotrexate.

III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet ALL initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Otrexup as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

Eloxatin (oxaliplatin)
oxaliplatin (generic)

POLICY

A. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Oxaliplatin, used in combination with infusional 5-fluorouracil/leucovorin, is indicated for:
1. Adjuvant treatment of stage III colon cancer in patients who have undergone complete resection of the primary tumor
2. Treatment of advanced colorectal cancer

Compendial Uses
1. Colorectal cancer
2. Esophageal or esophagogastric junction cancers
3. Gastric cancer
4. Hepatobiliary cancers
   • Extrahepatic cholangiocarcinoma
   • Intrahepatic cholangiocarcinoma
   • Gallbladder cancer
5. Neuroendocrine tumors of the pancreas
7. Occult primary cancer
8. Ovarian cancer (epithelial), fallopian tube cancer, primary peritoneal cancer, and mucinous carcinoma
9. Pancreatic adenocarcinoma
10. Testicular cancer
11. Non-Urothelial and Urothelial cancer with variant histology
12. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL)
13. Anal carcinoma

All other indications are considered experimental/investigational and are not a covered benefit.

B. CRITERIA FOR INITIAL APPROVAL

1. Colon and Rectal Cancer
   Authorization of 12 months may be granted for the treatment of colon and rectal cancers.

2. Pancreatic Adenocarcinoma
   Authorization of 12 months may be granted for the treatment of pancreatic adenocarcinoma.

3. Esophageal and Esophagogastric Junction Cancers
   Authorization of 12 months may be granted for the treatment of esophageal and esophagogastric junction cancers.
4. **Gastric Cancer**  
Authorization of 12 months may be granted for the treatment of gastric cancer.

5. **Intrahepatic and Extrahepatic Cholangiocarcinoma and Gallbladder Cancer**  
Authorization of 12 months may be granted for the treatment of intrahepatic and extrahepatic cholangiocarcinoma and gallbladder cancer.

6. **Neuroendocrine Tumors of the Pancreas**  
Authorization of 12 months may be granted for the treatment of neuroendocrine tumors of the pancreas.

7. **Non-Hodgkin’s Lymphoma (NHL)**  
Authorization of 12 months may be granted for the treatment of NHL.

8. **Occult Primary Tumors (cancer of unknown primary)**  
Authorization for 12 months may be granted for the treatment of occult primary tumors.

9. **Epithelial Ovarian Cancer, Fallopian Tube Cancer, Primary Peritoneal Cancer, and Mucinous Carcinoma**  
Authorization of 12 months may be granted for the treatment of epithelial ovarian cancer, fallopian tube cancer, primary peritoneal cancer, and mucinous carcinoma.

10. **Testicular Cancer**  
Authorization of 12 months may be granted for the treatment of testicular cancer.

11. **Non-Urothelial and Urothelial cancer with variant histology**  
Authorization of 12 months may be granted for the treatment of non-urothelial and urothelial cancer with variant histology.

12. **Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL)**  
Authorization of 12 months may be granted for the treatment of CLL/SLL.

13. **Anal Carcinoma**  
Authorization of 12 months may be granted for the treatment of anal cancer.

C. **CONTINUATION OF THERAPY**  
All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria.

D. **REFERENCES**
SPECIALTY GUIDELINE MANAGEMENT

OXERVATE (cenegermin-bkbj)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Oxervate is a recombinant human nerve growth factor indicated for the treatment of neurotrophic keratitis.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Neurotrophic keratitis

Authorization of 8 weeks may be granted for treatment of neurotrophic keratitis when all of the following criteria are met:

A. The patient must experience persistent epithelial defects (PED) or corneal ulceration of at least 2 weeks duration refractory to one or more conventional non-surgical treatments (e.g., preservative free artificial tears).

B. Evidence of decreased corneal sensitivity (less than or equal to 4 cm using the Cochet-Bonnet aesthesiometer) within the area of the PED or corneal ulcer and outside of the area of the defect in at least one corneal quadrant.

C. Performance of Schirmer test without anesthesia resulting in greater than 3 mm of moisture in 5 minutes

D. The patient has not received a previous course of Oxervate in the affected eye.

REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

PALYNZIQ (pegvaliase-pqpz)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Palynziq is indicated to reduce blood phenylalanine concentrations in adult patients with phenylketonuria who have uncontrolled blood phenylalanine concentrations greater than 600 micromol/L on existing management.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Phenylketonuria (PKU)¹²
Authorization of 6 months may be granted for members when baseline blood phenylalanine concentration, prior to initiation of the requested medication, is greater than 600 micromol/L.

III. CONTINUATION OF THERAPY

Phenylketonuria (PKU)
A. Authorization of indefinite approval may be granted for members who have achieved a clinical response as evidenced by either of the following:
   1. Member experienced a reduction in blood phenylalanine concentration of at least 20% from pre-treatment baseline.
   2. Member achieved a blood phenylalanine concentration of less than or equal to 600 micromol/L.

Phenylketonuria (PKU)
B. Authorization of 6 months may be granted for members who have not achieved a clinical response to treatment with Palynziq (at least a 20% reduction in blood phenylalanine concentration from pre-treatment baseline or a blood phenylalanine concentration less than or equal to 600 micromol/L) and meets one of the following requirements:
   1. Member has not been titrated to the maximum allowed dose of 40mg once daily.
   2. Member has received less than 16 weeks of continuous treatment at the maximum allowed dose.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

PARSABIV (etelcalcetide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Secondary hyperparathyroidism in adult patients with chronic kidney disease (CKD) on hemodialysis

All other indications are considered experimental/investigational and are not a covered benefit.

II. INITIAL CRITERIA FOR APPROVAL

Secondary hyperparathyroidism with CKD on hemodialysis
Authorization of 12 months may be granted for treatment of secondary hyperparathyroidism in a member with chronic kidney disease on hemodialysis who has a serum calcium level (corrected for albumin) greater than or equal to 8.3 mg/dL (see Appendix).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when the member is experiencing benefit from therapy as evidenced by a decrease in intact parathyroid hormone (iPTH) levels from pretreatment baseline.

IV. APPENDIX

Corrected calcium = measured total calcium + 0.8(4.0 – serum albumin)

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

PCSK9i
PRALUENT (alirocumab), REPATHA (evolocumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. Members with established atherosclerotic cardiovascular disease.
B. Members with an untreated LDL-C of greater than, or equal to, 190 mg/dL.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Clinical atherosclerotic cardiovascular disease (ASCVD)
   Authorization of 12 months may be granted when all of the following criteria are met:
   1. The member has a history of clinical atherosclerotic cardiovascular disease or has experienced a cardiovascular event
   2. The member has a current LDL-C level greater than, or equal to, 70 mg/dL
   3. The member is receiving maximally tolerated statin therapy or is statin intolerant

B. Primary or familial hyperlipidemia
   Authorization of 12 months may be granted when all of the following criteria are met:
   1. The member had an untreated (before any lipid lowering therapy) LDL-C level greater than, or equal to, 190 mg/dL
   2. The member has a current LDL-C level greater than, or equal to, 100 mg/dL
   3. The member is receiving maximally tolerated statin therapy or is statin intolerant

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members who are continuing therapy with a PCSK9i.

IV. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

PEGASYS (peginterferon alfa-2a)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Chronic Hepatitis C
      Pegasys, as part of a combination regimen with other hepatitis C virus (HCV) antiviral drugs, is indicated for the treatment of adults with chronic hepatitis C (CHC) with compensated liver disease. Pegasys in combination with ribavirin is indicated for treatment of pediatric patients 5 years of age and older with CHC and compensated liver disease. Pegasys monotherapy is only indicated for the treatment of patients with CHC with compensated liver disease if there are contraindications or significant intolerance to other HCV antiviral drugs.
   2. Chronic Hepatitis B
      Pegasys is indicated for the treatment of adult patients with HBeAg-positive and HBeAg-negative chronic hepatitis B infection who have compensated liver disease and evidence of viral replication and liver inflammation. Pegasys is indicated for the treatment of HBeAG-positive CHB in non-cirrhotic pediatric patients 3 years of age and older with evidence of viral replication and elevations in serum alanine.

B. Compendial Uses
   1. Myeloproliferative neoplasm (essential thrombocythemia, polycythemia vera, primary myelofibrosis and post-polycythemia vera or post-essential thrombocythemia myelofibrosis)
   2. Systemic mastocytosis

All other indications are considered experimental/investigational and are not a covered benefit.

II. INITIAL CRITERIA FOR APPROVAL

A. Chronic hepatitis C virus (HCV) infection
   Refer to the SGM of requested regimen for the specific criteria for approval and approval durations.

B. Chronic hepatitis B virus (HBV) infection (including HDV coinfection)
   Authorization of up to 48 weeks total may be granted for the treatment of chronic HBV infection, including HDV coinfection.

C. Myeloproliferative neoplasm
   Authorization of 12 months may be granted for the treatment of myeloproliferative neoplasm (essential thrombocythemia, polycythemia vera, primary myelofibrosis and post-polycythemia vera or post-essential thrombocythemia myelofibrosis).

D. Systemic mastocytosis
   Authorization of 12 months may be granted for the treatment of systemic mastocytosis.

III. CONTINUATION OF THERAPY

This document contains confidential and proprietary information of CVS Caremark and cannot be reproduced, distributed or printed without written permission from CVS Caremark. This document contains prescription brand name drugs that are trademarks or registered trademarks of pharmaceutical manufacturers that are not affiliated with CVS Caremark.
A. Myeloproliferative neoplasm
   Authorization of 12 months may be granted if the patient is experiencing benefit from therapy as evidenced by improvement in symptoms and/or disease markers (e.g., morphological response, reduction or stabilization in spleen size, improvement of thrombocytosis/leucocytosis, etc.)

B. Systemic mastocytosis
   Authorization of 12 months may be granted if the patient is experiencing benefit from therapy as evidenced by improvement in symptoms and/or disease markers (e.g., reduction in serum and urine metabolites of mast cell activation, improvement in cutaneous lesions, skeletal disease, bone marrow mast cell burden, etc.)

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

PERJETA (pertuzumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Metastatic breast cancer
   In combination with trastuzumab and docetaxel for the treatment of patients with human epidermal growth factor receptor 2 (HER2)-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.

2. Neoadjuvant treatment of breast cancer
   In combination with trastuzumab and chemotherapy as neoadjuvant treatment of patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer (either greater than 2 cm in diameter or node positive) as part of a complete treatment regimen for early breast cancer.

3. Adjuvant treatment of breast cancer
   In combination with trastuzumab and chemotherapy as adjuvant treatment of patients with HER2-positive early breast cancer at high risk of recurrence.

B. Compendial Uses

   Treatment of recurrent or stage IV (M1) human epidermal growth factor receptor 2 (HER2)-positive breast cancer

   All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

   Breast cancer

   A. Authorization of 6 months may be granted for neoadjuvant therapy of HER2-positive breast cancer.
   B. Authorization of 12 months may be granted for adjuvant therapy of HER2-positive breast cancer.
   C. Authorizations of 12 months may be granted for the treatment of recurrent or metastatic HER2-positive breast cancer.

III. CONTINUATION OF THERAPY

   All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria.
IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

BUPHENYL (sodium phenylbutyrate)
sodium phenylbutyrate (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Buphenyl is indicated as adjunctive therapy in the chronic management of patients with urea cycle disorders involving deficiencies of carbamylphosphate synthetase (CPS), ornithine transcarbamylase (OTC), or argininosuccinic acid synthetase (AS). It is indicated in all patients with neonatal-onset deficiency (complete enzymatic deficiency, presenting within the first 28 days of life). It is also indicated in patients with late-onset disease (partial enzymatic deficiency, presenting after the first month of life) who have a history of hyperammonemic encephalopathy. It is important that the diagnosis be made early and treatment initiated immediately to improve survival. Any episode of acute hyperammonemia should be treated as a life-threatening emergency.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of indefinite approval may be granted for chronic management of urea cycle disorder (UCD) when the diagnosis is confirmed by enzymatic, biochemical, or genetic testing.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

PIQRAY (alpelisib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Piqray is indicated in combination with fulvestrant for the treatment of postmenopausal women, and men, with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, PIK3CA-mutated, advanced or metastatic breast cancer as detected by an FDA-approved test following progression on or after an endocrine-based regimen.

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Documentation of FDA-approved test confirming presence of PIK3CA mutation.

III. CRITERIA FOR INITIAL APPROVAL

Breast cancer

Authorization of 12 months may be granted for treatment of HR-positive, HER2-negative, PIK3CA-mutated advanced or metastatic breast cancer when all of the following criteria are met:
A. Piqray is used in combination with fulvestrant
B. Disease has progressed while on or after an endocrine-based regimen

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

PLEGRIDY (peginterferon beta-1a)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications are considered covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

**FDA-Approved Indication:**
Plegridy is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

All other indications are considered experimental/investigational and are not covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Relapsing forms of multiple sclerosis
   Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

B. Clinically isolated syndrome
   Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome of multiple sclerosis.

III. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted for members who are experiencing disease stability or improvement while receiving Plegridy.

IV. OTHER CRITERIA

Members will not use Plegridy concomitantly with other medications used for the treatment of multiple sclerosis, excluding Ampyra.

V. REFERENCE

SPECIALTY GUIDELINE MANAGEMENT

POLIVY (polatuzumab vedotin-piiq)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Polivy in combination with bendamustine and a rituximab product is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, after at least two prior therapies.

B. Compendial Uses

1. High-grade B-cell lymphomas (HGBLs) with translocations of MYC and BCL2 and/or BCL6 after 2 or more prior therapies
2. Partially responsive, nonresponsive, or progressive DLBCL

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review for coverage of high-grade B cell lymphomas (HGBLs): Documentation of MYC and BCL2 and/or BCL6 translocations as detected by fluorescence in situ hybridization (FISH) or standard cytogenetics.

III. CRITERIA FOR INITIAL APPROVAL

A. Diffuse large B-cell lymphoma

Authorization of 6 months may be granted for treatment of diffuse large B-cell lymphoma (DLBCL) when all of the following criteria are met:
1. Polivy is used in combination with bendamustine and a rituximab product
2. Disease is partially responsive, not responsive, relapsed, refractory, or progressive after prior therapies
3. Member has received at least two prior therapies
4. Member will not receive more than 6 cycles of therapy
5. Member is not a candidate for transplant

B. High-grade B-cell lymphomas (HGBLs)

Authorization of 6 months may be granted for treatment of high-grade B-cell lymphomas (HGBLs) (also referred to as “double-hit” or “triple-hit” lymphomas) when all of the following criteria are met:
1. Member has translocations of MYC and BCL2 and/or BCL6 as detected by FISH or standard cytogenetics
2. Polivy is used in combination with bendamustine and a rituximab product
3. Disease is partially responsive, not responsive, relapsed, refractory, or progressive after prior therapies
4. Member has received at least two prior therapies
5. Member will not receive more than 6 cycles of therapy
6. Member is not a candidate for transplant

IV. CONTINUATION OF THERAPY

Authorization up to 6 months (6 cycles total) may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced disease progression or an unacceptable toxicity and who have not received 6 or more cycles of Polivy.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

POMALYST (pomalidomide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
   Treatment of multiple myeloma, in combination with dexamethasone, in patients who have received at least two prior therapies including lenalidomide and a proteasome inhibitor and have demonstrated disease progression on or within 60 days of completion of their last therapy.

B. Compendial Uses
   1. Systemic light chain amyloidosis
   2. AIDS-related Kaposi sarcoma

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Multiple myeloma
   Authorization of 12 months may be granted for the treatment of multiple myeloma when the member has previously received at least two prior therapies for multiple myeloma.

B. Systemic light chain amyloidosis
   Authorization of 12 months may be granted for the treatment of systemic light chain amyloidosis.

C. AIDS-Related Kaposi Sarcoma
   Authorization of 12 months may be granted for the treatment of AIDS-related Kaposi sarcoma.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

PORTRAZZA (necitumumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication¹
Portrazza is indicated for the first-line treatment of patients with metastatic squamous non-small cell lung cancer (NSCLC) in combination with gemcitabine and cisplatin.

Limitation of Use: Portrazza is not indicated for the treatment of non-squamous non-small cell lung cancer.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Non-Small Cell Lung Cancer (NSCLC)¹
Authorization of 12 months may be granted for treatment of metastatic squamous NSCLC when the requested medication is used in combination with gemcitabine and cisplatin.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

POTELIGEO (mogamulizumab-kpkc)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Poteligo is indicated for the treatment of adult patients with relapsed or refractory mycosis fungoides (MF) or Sézary syndrome (SS) after at least one prior systemic therapy.

B. Compendial Uses

1. Mycosis fungoides (MF) or Sézary syndrome (SS) as primary treatment
2. Adult T-cell leukemia/lymphoma

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Mycosis fungoides (MF) or Sézary syndrome (SS)1,2

Authorization of 12 months may be granted for treatment of mycosis fungoides (MF) or Sézary syndrome (SS).

B. Adult T-cell leukemia/lymphoma1,2

Authorization of 12 months may be granted for treatment of adult T-cell leukemia/lymphoma.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>BRAND NAME</th>
<th>PRALUENT</th>
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<td>(generic)</td>
<td>(alirocumab)</td>
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Status: CVS Caremark Criteria

Type: Initial Prior Authorization

FDA-APPROVED INDICATIONS

- **Atherosclerotic cardiovascular disease**
  Praluent is indicated to reduce the risk of myocardial infarction, stroke, and unstable angina requiring hospitalization in adults with established cardiovascular disease.

- **Primary hyperlipidemia**
  Praluent is indicated as an adjunct to diet, alone or in combination with other lipid-lowering therapies (e.g., statins, ezetimibe) for the treatment of adults with primary hyperlipidemia (including heterozygous familial hypercholesterolemia) or to reduce low-density lipoprotein cholesterol (LDL-C).

CRITERIA FOR APPROVAL

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Mapping Instructions

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RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to ensure that patients follow selection elements noted in labeling and/or practice guidelines in order to decrease the potential for inappropriate utilization.

REFERENCES


ENHANCED SPECIALTY GUIDELINE MANAGEMENT

PRALUENT (alirocumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
A. Praluent is indicated to reduce the risk of myocardial infarction, stroke, and unstable angina in adults with established cardiovascular disease.
B. Praluent is indicated as an adjunct to diet, alone or in combination with other lipid-lowering therapies (e.g., statins, ezetimibe) for the treatment of adults with primary hyperlipidemia (including heterozygous familial hypercholesterolemia) to reduce low density lipoprotein cholesterol (LDL-C).

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

The following is necessary to initiate the prior authorization review:
A. Current LDL-C level for both initial requests and continuation requests. The level must be dated within the six months preceding the authorization request.
B. Untreated (before any lipid lowering therapy) LDL-C level if requesting Praluent to treat primary hyperlipidemia or heterozygous familial hypercholesterolemia.
C. Chart notes confirming clinical atherosclerotic cardiovascular disease (ASCVD) if requesting Praluent to treat clinical ASCVD.
D. If patient has contraindication or intolerance to statins, chart notes confirming the contraindication or intolerance. (See Appendix B and C).

III. CRITERIA FOR INITIAL APPROVAL

A. Clinical atherosclerotic cardiovascular disease (ASCVD)

Authorization of 6 months may be granted for treatment of clinical atherosclerotic cardiovascular disease when all of the following criteria are met:
1. Member has a history of clinical ASCVD (See Appendix A).
2. Member meets at least one of the following requirements:
   a. Member has a current LDL-C level $\geq 70$ mg/dL after at least three months of treatment with a high-intensity statin dose in combination with ezetimibe. If the member is unable to tolerate a high-intensity statin dose, a moderate-intensity statin dose may be used.
   b. Member has a current LDL-C level $\geq 70$ mg/dL with contraindication or intolerance to statins (See Appendix B and C).
B. Primary hyperlipidemia including heterozygous familial hypercholesterolemia (HeFH)

Authorization of 6 months may be granted for treatment of primary hyperlipidemia including heterozygous familial hypercholesterolemia (HeFH) when both of the following criteria are met:

1. Member had an untreated (before any lipid lowering therapy) LDL-C level ≥ 190 mg/dL in the absence of a secondary cause.

2. Member meets at least one of the following requirements:
   a. Member has a current LDL-C level ≥ 100 mg/dL after at least three months of treatment with a high-intensity statin dose in combination with ezetimibe. If the member is unable to tolerate a high-intensity statin dose, a moderate-intensity statin dose may be used.
   b. Member has a current LDL-C level ≥ 100 mg/dL with contraindication or intolerance to statins (See Appendix B and C).

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members who achieve or maintain an LDL-C reduction (e.g., LDL-C is now at goal, robust lowering of LDL-C).

V. APPENDICES

APPENDIX A. Clinical ASCVD
- Acute coronary syndromes
- Myocardial infarction
- Stable or unstable angina
- Coronary or other arterial revascularization procedure (e.g., percutaneous coronary angioplasty [PTCA], coronary artery bypass graft [CABG] surgery)
- Stroke of presumed atherosclerotic origin
- Transient ischemic attack (TIA)
- Non-cardiac peripheral arterial disease of presumed atherosclerotic origin (e.g., carotid artery stenosis, lower extremity PAD)
- Obstructive coronary artery disease (defined as fifty percent or greater stenosis on cardiac computed tomography angiogram or catheterization)

APPENDIX B. Statin-associated muscle symptoms (SAMS) and statin re-challenge
- Score of 7 or higher on the Statin-Associated Muscle Symptom Clinical Index (SAMS-CI)
- Statin-associated elevation in creatine kinase (CK) level ≥ 10 times upper limit of normal (ULN)

**NOTE**: Statin re-challenge is NOT required for members who have experienced an elevation of CK level ≥10 times ULN after receiving lipid-lowering therapy (LLT) with a statin.

APPENDIX C. Contraindications to statins
- Active liver disease, including unexplained persistent elevations in hepatic transaminase levels (e.g., alanine transaminase (ALT) level ≥ 3 times ULN)
- Pregnancy or planned pregnancy
- Breastfeeding

VI. REFERENCES


PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
  (generic)  (pretomanid)

Status:  CVS Caremark Criteria
Type: Initial Prior Authorization

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS
Limited Population: Pretomanid Tablet is indicated, as part of a combination regimen with bedaquiline and linezolid for the treatment of adults with pulmonary extensively drug resistant (XDR) or treatment-intolerant or nonresponsive multidrug-resistant (MDR) tuberculosis (TB). Approval of this indication is based on limited clinical safety and efficacy data. This drug is indicated for use in a limited and specific population of patients.

Limitations of Use:
• Pretomanid Tablets are not indicated in patients with the following conditions:
  o Drug-sensitive (DS) tuberculosis
  o Latent infection due to Mycobacterium tuberculosis.
  o Extra-pulmonary infection due to Mycobacterium tuberculosis.
  o MDR-TB that is not treatment-intolerant or nonresponsive to standard therapy.

• Safety and effectiveness of Pretomanid Tablets have not been established for its use in combination with drugs other than bedaquiline and linezolid as part of the recommended dosing regimen.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:
• The requested drug is being prescribed for pulmonary extensively-drug resistant (XDR) or treatment-intolerant/nonresponsive multidrug-resistant (MDR) tuberculosis
AND
• The requested drug will be prescribed as part of a combination regimen with Sirturo (bedaquiline) and Zyvox (linezolid)

RATIONALE
The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Pretomanid Tablet is indicated, as part of a combination regimen with bedaquiline and linezolid for the treatment of adults with pulmonary extensively drug resistant (XDR) or treatment-intolerant or nonresponsive multidrug-resistant (MDR) tuberculosis (TB). This drug is indicated for use in a limited and specific population of patients.

Safety and effectiveness of Pretomanid Tablets have not been established for its use in combination with drugs other than bedaquiline and linezolid as part of the recommended dosing regimen. Pretomanid Tablets must be used only in combination with bedaquiline and linezolid as part of the recommended dosing regimen. The recommended dosage and duration for this combination regimen are as follows:
• Pretomanid Tablet 200 mg orally (1 tablet of 200 mg), once daily, for 26 weeks. Swallow Pretomanid Tablets whole with water
• Bedaquiline 400 mg orally once daily for 2 weeks followed by 200 mg 3 times per week, with at least 48 hours between doses, for 24 weeks for a total of 26 weeks
If either bedaquiline or Pretomanid Tablets are discontinued, the entire combination regimen should also be discontinued.
• Linezolid starting at 1,200 mg orally per day for 26 weeks, with dose adjustments to 600 mg daily and further reduction to 300 mg daily or interruption of dosing as necessary for known linezolid adverse reactions of myelosuppression, peripheral neuropathy, and optic neuropathy.
If linezolid is permanently discontinued during the initial four consecutive weeks of treatment, bedaquiline and Pretomanid Tablets should also be discontinued. If linezolid is discontinued after the initial four weeks of consecutive treatment, continue administering bedaquiline and Pretomanid Tablets.

The duration of approval is set at 12 months since that the dosing of the combination regimen of Pretomanid, bedaquiline, and linezolid can be extended beyond 26 weeks, if necessary.\textsuperscript{1-3}

REFERENCES

CRITERIA FOR APPROVAL

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Mapping Instructions

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SPECIALTY GUIDELINE MANAGEMENT

PROCYSBI (cysteamine bitartrate delayed-release)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Procysbi is indicated for the treatment of nephropathic cystinosis in adults and pediatric patients 1 year of age and older.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Nephropathic cystinosis
Indefinite authorization may be granted for treatment of nephropathic cystinosis when all of the following criteria are met:
A. Diagnosis of cystinosis was confirmed by the presence of increased cystine concentration in leukocytes or by genetic testing
B. Member is 1 year of age or older

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

PROLEUKIN (aldesleukin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Proleukin is indicated for the treatment of adults with metastatic renal cell carcinoma (metastatic RCC).
   2. Proleukin is indicated for the treatment of adults with metastatic melanoma.

B. Compendial Uses
   1. Relapsed or stage IV kidney cancer with clear cell histology; as high-dose single-agent therapy as first-line or subsequent therapy
   2. Metastatic or unresectable cutaneous melanoma; as high-dose single-agent therapy as second-line or subsequent therapy
   3. Neuroblastoma

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Renal Cell Carcinoma
   Authorization of 12 months may be granted for treatment of relapsed or metastatic renal cell carcinoma with clear cell histology for high-dose single-agent therapy as first-line or subsequent therapy.

B. Melanoma
   Authorization of 12 months may be granted for treatment of metastatic or unresectable cutaneous melanoma for high-dose single-agent therapy as second-line or subsequent therapy.

C. Neuroblastoma
   Authorization of 12 months may be granted for the treatment of neuroblastoma.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when all of the following criteria are met:
1. The member must be evaluated for response approximately 4 weeks after completion of a course of therapy and again immediately prior to the scheduled start of the next treatment course,
2. Additional courses of treatment should be given only if there is some tumor shrinkage following the last course,
3. Retreatment is not contraindicated,
4. Each treatment course should be separated by a rest period of at least 7 weeks from the date of hospital discharge.

IV. REFERENCES

4. Russell HV, Shohet JM, Nuchtern JG. Treatment and prognosis of neuroblastoma. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed September 2012.
SPECIALTY GUIDELINE MANAGEMENT

PROLIA (denosumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Treatment of postmenopausal women with osteoporosis at high risk for fracture
   2. Treatment to increase bone mass in men with osteoporosis at high risk for fracture
   3. Treatment of men and women with glucocorticoid-induced osteoporosis at high risk for fracture
   4. Treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy (ADT) for non-metastatic prostate cancer
   5. Treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer

B. Compendial Uses
   Prevention or treatment of osteoporosis during androgen deprivation therapy for prostate cancer in patients with high fracture risk

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Supporting chart notes or medical record indicating a history of fractures, T-score, and FRAX fracture probability as applicable to Sections III.A, III.B, and III.C.

III. CRITERIA FOR INITIAL APPROVAL

A. Postmenopausal osteoporosis
   Authorization of 12 months may be granted to postmenopausal members with osteoporosis when ANY of the following criteria are met:
   1. Member has a history of fragility fractures
   2. Member has a pre-treatment T-score less than or equal to -2.5 OR member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B) and meets ANY of the following criteria:
      a. Member has indicators of higher fracture risk (e.g., advanced age, frailty, glucocorticoid use, very low T-scores [less than or equal to -3.5], or increased fall risk)
      b. Member has failed prior treatment with or is intolerant to previous injectable osteoporosis therapy (e.g., zoledronic acid [Reclast], teriparatide [Forteo])
c. Member has had an oral bisphosphonate trial of at least 1-year duration or there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)

B. Osteoporosis in men
Authorization of 12 months may be granted to male members with osteoporosis when ANY of the following criteria are met:
1. Member has a history of an osteoporotic vertebral or hip fracture
2. Member meets criteria BOTH of the following criteria:
   a. Member has a pre-treatment T-score less than or equal to -2.5 OR member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B)
   b. Member has had an oral bisphosphonate trial of at least 1-year duration OR there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)

C. Glucocorticoid-induced osteoporosis
Authorization of 12 months may be granted to members with glucocorticoid-induced osteoporosis when ALL of the following criteria are met:
1. Member is currently receiving or will be initiating glucocorticoid therapy
2. Member has had an oral bisphosphonate trial of at least 1-year duration OR there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)
3. Member meets ANY of the following criteria:
   a. Member has a history of a fragility fracture
   b. Member has a pre-treatment T-score less than or equal to -2.5
   c. Member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B)

D. Breast cancer
Authorization of 12 months may be granted to members who are receiving adjuvant aromatase inhibitor therapy for breast cancer.

E. Prostate cancer
Authorization of 12 months may be granted to members who are receiving androgen deprivation therapy for prostate cancer.

IV. CONTINUATION OF THERAPY
Authorization of 12 months may be granted for all members (including new members) who meet all initial authorization criteria and experiences clinical benefit after at least 24 months of therapy with Prolia as evidenced by improvement or stabilization in T-score.

V. APPENDIX
Appendix A. Clinical reasons to avoid oral bisphosphonate therapy
- Esophageal abnormality that delays emptying such as stricture of achalasia
- Active upper gastrointestinal problem (e.g., dysphagia, gastritis, duodenitis, erosive esophagitis, ulcers)
- Inability to stand or sit upright for at least 30 to 60 minutes
- Inability to take at least 30 to 60 minutes before first food, drink, or medication of the day
- Renal insufficiency (creatinine clearance <35 mL/min)
• History of intolerance to an oral bisphosphonate

Appendix B. WHO Fracture Risk Assessment Tool
• High FRAX fracture probability: 10 year major osteoporotic fracture risk ≥ 20% or hip fracture risk ≥ 3%.
• 10-year probability; calculation tool available at: https://www.sheffield.ac.uk/FRAX/
• The estimated risk score generated with FRAX should be multiplied by 1.15 for major osteoporotic fracture and 1.2 for hip fracture if glucocorticoid treatment is greater than 7.5 mg per day.

VI. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

PROMACTA (eltrombopag)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Treatment of thrombocytopenia in adult and pediatric patients 1 year and older with chronic immune (idiopathic) thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy
   2. Treatment of thrombocytopenia in patients with chronic hepatitis C to allow the initiation and maintenance of interferon-based therapy
   3. First-line treatment of severe aplastic anemia in adult and pediatric patients 2 years and older in combination with standard immunosuppressive therapy.
   4. Treatment of patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy

B. Compendial Use
   1. MYH9-related disease with thrombocytopenia

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Chronic or persistent primary immune thrombocytopenia (ITP)
   Authorization of 6 months may be granted to members with chronic or persistent ITP who meet all of the following criteria:
   1. Inadequate response or intolerance to documented prior therapy with corticosteroids, immunoglobulins, or splenectomy
   2. Untransfused platelet count at time of diagnosis is less than 30x10⁹/L OR 30x10⁹/L to 50x10⁹/L with symptomatic bleeding (e.g., significant mucous membrane bleeding, gastrointestinal bleeding or trauma) or risk factors for bleeding (see Section IV).

B. Thrombocytopenia associated with chronic hepatitis C
   Authorization of 6 months may be granted to members who are prescribed Promacta for the initiation and maintenance of interferon-based therapy for the treatment of thrombocytopenia associated with chronic hepatitis C.

C. Aplastic anemia
   1. Authorization of 6 months may be granted to members for the first-line treatment of severe aplastic anemia when Promacta will be used in combination with standard immunosuppressive therapy (e.g. horse antithymocyte globulin (h-ATG) and cyclosporine).
2. Authorization of 6 months may be granted to members for the treatment of aplastic anemia which has been previously treated with immunosuppressive therapy.

D. MYH9-related disease with thrombocytopenia
   Authorization of 12 months may be granted to members with thrombocytopenia associated with MYH9-related disease.

III. CONTINUATION OF THERAPY

A. Chronic or persistent ITP
   1. Authorization of 12 months may be granted to members with current platelet count less than or equal to 200x10^9/L.
   2. Authorization of 12 months may be granted to members with current platelet count greater than 200 x10^9/L for whom Promacta dosing will be adjusted to achieve a platelet count sufficient to avoid clinically important bleeding.

B. Thrombocytopenia associated with chronic hepatitis C
   Authorization of 6 months may be granted to members who are continuing to receive interferon-based therapy.

C. Aplastic anemia
   1. Authorization of up to 16 weeks total may be granted to members with current platelet count less than 50x10^9/L who have not received appropriately titrated therapy with Promacta for at least 16 weeks.
   2. Authorization of up to 16 weeks total may be granted to members with current platelet count less than 50x10^9/L who are transfusion-independent.
   3. Authorization of 12 months may be granted to members with current platelet count of 50x10^9/L to 200x10^9/L.
   4. Authorization of 12 months may be granted to members with current platelet count greater than 200 x10^9/L for whom Promacta dosing will be adjusted to achieve and maintain an appropriate target platelet count.

D. MYH9-related disease with thrombocytopenia
   All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. APPENDIX

Examples of risk factors for bleeding (not all inclusive)
   • Undergoing a medical or dental procedure where blood loss is anticipated
   • Comorbidity (e.g., peptic ulcer disease, hypertension)
   • Mandated anticoagulation therapy
   • Profession (e.g., construction worker) or lifestyle (e.g., plays contact sports) that predisposes patient to trauma

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

PULMOZYME (dornase alfa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Pulmozyme is indicated in conjunction with standard therapies for the management of cystic fibrosis (CF) patients to improve pulmonary function.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Cystic Fibrosis
Authorization of 24 months may be granted for treatment of cystic fibrosis when Pulmozyme will be used in conjunction with standard therapies for cystic fibrosis.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

### PRIOR AUTHORIZATION CRITERIA

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**Status:** CVS Caremark Criteria  
**Type:** Initial Prior Authorization  
**Ref #** 794-A

*Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

**FDA-APPROVED INDICATIONS**

Qsymia is indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adult patients with an initial body mass index (BMI) of

- 30 kg/m² or greater (obese), or
- 27 kg/m² or greater (overweight) in the presence of at least one weight related comorbidity such as hypertension, type 2 diabetes mellitus, or dyslipidemia

**Limitations of Use**

- The effect of Qsymia on cardiovascular morbidity and mortality has not been established.
- The safety and effectiveness of Qsymia in combination with other products intended for weight loss, including prescription and over-the-counter drugs and herbal preparations have not been established.

**COVERAGE CRITERIA**

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has completed at least 12 weeks of Qsymia 15 mg/92 mg therapy AND
  - The patient lost at least 5 percent of baseline body weight OR the patient has continued to maintain their initial 5 percent weight loss
  OR
- The patient has completed at least 12 weeks of Qsymia 7.5 mg/46 mg therapy AND
  - The patient lost at least 3 percent of baseline body weight OR the patient’s dose will be escalated
  OR
- The requested drug will be used with a reduced calorie diet and increased physical activity AND
  - The patient has a body mass index (BMI) greater than or equal to 30 kg per square meter
    OR
  - The patient has a body mass index (BMI) greater than or equal to 27 kg per square meter AND has additional risk factors

**RATIONALE**

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Qsymia is indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adult patients with an initial body mass index (BMI) of 30 kg/m² or greater (obese), or 27 kg/m² or greater (overweight) in the presence of at least one weight related comorbidity such as hypertension, type 2 diabetes mellitus, or dyslipidemia. The effect of Qsymia on cardiovascular morbidity and mortality has not been established. The safety and effectiveness of Qsymia in combination with other products intended for weight loss, including prescription and over-the-counter drugs and herbal preparations have not been established.
The guidelines state that the purpose of weight loss and weight maintenance is to reduce health risk. Weight loss programs should begin with a basic weight loss regimen consisting of a reduced-calorie diet and increased physical activity. The major role of medications is to help with patient compliance to a weight loss plan. Therefore, drugs should be used as part of a comprehensive weight loss program and should never be used without concomitant lifestyle modification. Drugs may be used as an adjunct to diet and physical activity for patients with a BMI that is greater than or equal to 30 kg/m² or greater than or equal to 27 kg/m² if other risk factors are present (e.g., hypertension, diabetes, dyslipidemia, sleep apnea, cardiovascular disease).4-6

Qsymia is to be taken once daily in the morning. Treatment should begin with Qsymia 3.75 mg/23 mg daily for 14 days. After 14 days, it is recommended to increase the dose to Qsymia 7.5 mg/46 mg. The patient should be evaluated at 12 weeks. If the patient has not lost 3% of baseline body weight on 7.5 mg/46 mg, Qsymia should be discontinued or the dose should be escalated, as it is unlikely that the patient will achieve and sustain clinically meaningful weight loss at the Qsymia 7.5 mg/46 mg dose. The dose should be escalated to Qsymia 11.25 mg/69 mg daily for 14 days, followed by Qsymia 15 mg/92 mg daily. The patient should then be evaluated after 12 weeks. If the patient has not lost at least 5% of baseline body weight, Qsymia treatment should be discontinued.

For renewal after 12 weeks of therapy, the patient must have lost at least 5% of their baseline body weight or has continued to maintain their initial 5 percent weight loss. It is recommended that therapy be discontinued after 12 weeks if the patient does not meet this goal, as it is unlikely that the patient will be able to achieve and sustain clinically meaningful weight loss with continued treatment.1

The optimal duration of treatment is unclear. Considering that drug discontinuation invariably leads to weight regain, if clinically significant weight loss is achieved, longer courses of treatment are reasonable to consider after the benefits and risks of treatment are reviewed with the patient and lack of long-term data is acknowledged.4-6

REFERENCES
Has the patient completed at least 12 weeks of Qsymia 7.5 mg/46 mg therapy?  
[If no, then skip to question 5.]  
Yes  No

Did the patient lose at least 3 percent of baseline body weight or will the patient’s dose be escalated?  
[No further questions.]  
Yes  No

Did the patient lose at least 5 percent of baseline body weight OR has the patient continued to maintain their initial 5 percent weight loss?  
[No further questions.]  
Yes  No

Does the patient have a body mass index (BMI) greater than or equal to 30 kg per square meter?  
[If yes, then skip to question 7.]  
Yes  No

Does the patient have a body mass index (BMI) greater than or equal to 27 kg per square meter AND has additional risk factors?  
Yes  No

Will the requested medication be used with a reduced calorie diet and increased physical activity?  
Yes  No

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**Guidelines for Approval**

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<td>You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions: - You have a body mass index (BMI) of 30 kg per square meter or more - You have a body mass index (BMI) of 27 kg per square meter or more and you have risk factors Your request has been denied based on the information we have. [Short Description: Not at BMI requirement]</td>
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<td>You do not meet the requirements of your plan. Your plan covers this drug when you will diet and exercise. Your request has been denied based on the information we have. [Short Description: Diet and exercise requirement not met]</td>
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SPECIALTY GUIDELINE MANAGEMENT

RADICAVA (edaravone)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Radicava is indicated for the treatment of amyotrophic lateral sclerosis (ALS).

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of ALS when all of the following criteria are met:
A. Diagnosis of definite or probable ALS
B. Member has scores of at least 2 points on all 12 areas of the revised ALS Functional Rating Scale (ALSFRS-R)
C. Continuous use of ventilatory support during the day and night is not required (noninvasive or invasive)

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members continuing with Radicava therapy for the treatment of ALS when the following criteria are met:
A. Diagnosis of definite or probable ALS
B. There is a clinical benefit from Radicava therapy
C. Invasive ventilation is not required

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

RASUVO (methotrexate injection)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Rheumatoid Arthritis including Polyarticular Juvenile Idiopathic Arthritis
   Rasuvo is indicated in the management of selected adults with severe, active rheumatoid arthritis (RA) or children with active polyarticular juvenile idiopathic arthritis, who have had an insufficient therapeutic response to, or are intolerant of, an adequate trial of first-line therapy including full dose non-steroidal anti-inflammatory agents (NSAIDs).

2. Psoriasis
   Rasuvo is indicated in adults for the symptomatic control of severe, recalcitrant, disabling psoriasis that is not adequately responsive to other forms of therapy, but only when the diagnosis has been established, as by biopsy and/or after dermatologic consultation. It is important to ensure that a psoriasis “flare” is not due to an undiagnosed concomitant disease affecting immune responses.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 24 months may be granted for treatment of RA, pJIA, or psoriasis when BOTH of the following criteria are met:

A. Member has tried and had an inadequate response or intolerance to generic oral methotrexate.

B. Member has inability to prepare and administer generic injectable methotrexate.

III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet ALL initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Rasuvo as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

RAVICTI (glycerol phenylbutyrate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Ravicti is indicated for the chronic management of patients with urea cycle disorders (UCDs) who cannot be managed by dietary protein restriction and/or amino acid supplementation alone. Ravicti must be used with dietary protein restriction and, in some cases, dietary supplements.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Authorizations of indefinite approval may be granted for chronic management of a urea cycle disorder (UCD) when the diagnosis is confirmed by enzymatic, biochemical, or genetic testing.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

REBIF (interferon beta-1a)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Rebif is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

Compendial Use
First clinical episode of multiple sclerosis with magnetic resonance imaging features consistent with multiple sclerosis

All other indications are considered experimental/investigational and are not covered benefits.

II. CRITERIA FOR INITIAL APPROVAL

A. Relapsing forms of multiple sclerosis
   Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

B. Clinically isolated syndrome
   Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome of multiple sclerosis.

III. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted for members who are experiencing disease stability or improvement while receiving Rebif.

IV. OTHER CRITERIA

Members will not use Rebif concomitantly with other medications used for the treatment of multiple sclerosis, excluding Ampyra.

V. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

REMICADE (infliximab)
INFLECTRA (infliximab-dyyb)
RENFLEXIS (infliximab-abda)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Moderately to severely active Crohn’s disease (CD)
   2. Moderately to severely active ulcerative colitis (UC)
   3. Moderately to severely active rheumatoid arthritis (RA) in combination with methotrexate
   4. Active ankylosing spondylitis (AS)
   5. Active psoriatic arthritis (PsA)
   6. Chronic severe plaque psoriasis (PsO)

B. Compendial Uses
   1. Axial spondyloarthritis
   2. Behçet’s syndrome
   3. Granulomatosis with polyangiitis (Wegener’s granulomatosis)
   4. Hidradenitis suppurativa
   5. Juvenile idiopathic arthritis
   6. Pyoderma gangrenosum
   7. Sarcoidosis
   8. Takayasu’s arteritis
   9. Uveitis

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active Crohn’s disease (CD)
   1. Authorization of 24 months may be granted for members who have previously received Remicade, Inflectra, Renflexis, or any other biologic indicated for the treatment of Crohn’s disease.

   2. Authorization of 24 months may be granted for treatment of moderately to severely active CD when any of the following criteria is met:
      a. Member has fistulizing disease.
      b. Member has an inadequate response, intolerance or contraindication to at least one conventional therapy option (see Appendix A).
B. Moderately to severely active ulcerative colitis (UC)
   1. Authorization of 24 months may be granted for members who have previously received Remicade, Inflectra, Renflexis, or any other biologic or targeted synthetic drug (e.g., Xeljanz) indicated for moderately to severely active ulcerative colitis.
   2. Authorization of 24 months may be granted for treatment of moderately to severely active UC when the member has an inadequate response, intolerance or contraindication to at least ONE conventional therapy option (see Appendix B).

C. Moderately to severely active rheumatoid arthritis (RA)
   1. Authorization of 24 months may be granted for members who have previously received Remicade, Inflectra, Renflexis, or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) indicated for moderately to severely active rheumatoid arthritis. Remicade, Inflectra, or Renflexis must be prescribed in combination with methotrexate or leflunomide unless the member has a clinical reason not to use methotrexate or leflunomide.
   2. Authorization of 24 months may be granted for treatment of moderately to severely active RA when all of the following criteria are met:
      a. Member is prescribed Remicade, Inflectra, or Renflexis in combination with methotrexate or leflunomide, or has a clinical reason not to use methotrexate or leflunomide.
      b. Member meets any of the following criteria:
         i. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
         ii. Member has an intolerance or contraindication to methotrexate (see Appendix C).

D. Active ankylosing spondylitis (AS) and axial spondyloarthritis
   1. Authorization of 24 months may be granted for members who have previously received Remicade, Inflectra, Renflexis, or any other biologic DMARD indicated for active ankylosing spondylitis.
   2. Authorization of 24 months may be granted for treatment of active ankylosing spondylitis and axial spondyloarthritis when any of the following criteria is met:
      a. Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs).
      b. Member has an intolerance or contraindication to two or more NSAIDs.

E. Active psoriatic arthritis (PsA)
   Authorization of 24 months may be granted for treatment of active psoriatic arthritis (PsA).

F. Chronic severe plaque psoriasis
   1. Authorization of 24 months may be granted for members who have previously received Remicade, Inflectra, Renflexis, Otezla, or any other biologic DMARD indicated for the treatment of chronic, severe plaque psoriasis.
   2. Authorization of 24 months may be granted for treatment of chronic severe plaque psoriasis when all of the following criteria are met:
      a. At least 5% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
      b. Member meets any of the following criteria:
         i. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
ii. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine or acitretin (see Appendix D).
iii. Member has severe psoriasis that warrants a biologic DMARD as first-line therapy.

G. Behçet’s syndrome
Authorization of 24 months may be granted for treatment of Behçet’s syndrome.

H. Granulomatosis with polyangiitis (Wegener’s granulomatosis)
Authorization of 24 months may be granted for treatment of granulomatosis with polyangiitis.

I. Hidradenitis suppurativa
Authorization of 24 months may be granted for treatment of severe, refractory hidradenitis suppurativa.

J. Juvenile Idiopathic arthritis (JIA)
1. Authorization of 24 months may be granted for members who have previously received Remicade, Inflectra, or Renflexis or any other biologic DMARD indicated for juvenile idiopathic arthritis.

2. Authorization of 24 months may be granted for treatment of JIA when any of the following criteria is met:
   a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate.
   b. Member has intolerance or contraindication to methotrexate (see Appendix C).

K. Pyoderma gangrenosum
Authorization of 24 months may be granted for treatment of pyoderma gangrenosum.

L. Sarcoidosis
Authorization of 24 months may be granted for treatment of sarcoidosis.

M. Takayasu’s arteritis
Authorization of 24 months may be granted for treatment of Takayasu’s arteritis.

N. Uveitis
Authorization of 24 months may be granted for treatment of uveitis in members who have experienced an inadequate response or intolerance or have a contraindication to a trial of immunosuppressive therapy for uveitis (e.g., methotrexate, azathioprine, or mycophenolate mofetil).

III. CONTINUATION OF THERAPY
Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Remicade, Inflectra, or Renflexis as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER
For all indications: Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB).
V. APPENDICES

Appendix A: Examples of Conventional Therapy Options for CD

1. Mild to moderate disease – induction of remission:
   a. Oral budesonide
   b. Alternatives: metronidazole, ciprofloxacin, rifaximin

2. Mild to moderate disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternatives: oral budesonide, methotrexate intramuscular (IM) or subcutaneous (SC), sulfasalazine

3. Moderate to severe disease – induction of remission:
   a. Prednisone, methylprednisolone intravenously (IV)
   b. Alternatives: methotrexate IM or SC

4. Moderate to severe disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: methotrexate IM or SC

5. Perianal and fistulizing disease – induction of remission:
   a. Metronidazole ± ciprofloxacin, tacrolimus

6. Perianal and fistulizing disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: methotrexate IM or SC

Appendix B: Examples of Conventional Therapy Options for UC

1. Mild to moderate disease – induction of remission:
   a. Oral mesalamine (e.g., Asacol, Asacol HD, Lialda, Pentasa), balsalazide, olsalazine
   b. Rectal mesalamine (e.g., Canasa, Rowasa)
   c. Rectal hydrocortisone (e.g., Colocort, Cortifoam)
   d. Alternatives: prednisone, azathioprine, mercaptopurine, sulfasalazine

2. Mild to moderate disease – maintenance of remission:
   a. Oral mesalamine, balsalazide, olsalazine, rectal mesalamine
   b. Alternatives: azathioprine, mercaptopurine, sulfasalazine

3. Severe disease – induction of remission:
   a. Prednisone, hydrocortisone IV, methylprednisolone IV
   b. Alternatives: cyclosporine IV, tacrolimus, sulfasalazine

4. Severe disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: sulfasalazine

5. Pouchitis: Metronidazole, ciprofloxacin
   a. Alternative: rectal mesalamine

Appendix C: Examples of Contraindications to Methotrexate

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy
10. Renal impairment
11. Significant drug interaction

Appendix D: Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin.
1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Drug interaction
4. Cannot be used due to risk of treatment-related toxicity
5. Pregnancy or planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VI. REFERENCES


PRIOR AUTHORIZATION CRITERIA

BRAND NAME REPATHA (generic) (evolocumab)

Status: CVS Caremark Criteria MDC Type: Initial Prior Authorization Ref # 1774-A

FDA-APPROVED INDICATIONS
Atherosclerotic cardiovascular disease
Repatha is indicated to reduce the risk of myocardial infarction, stroke, and coronary revascularization in adults with established cardiovascular disease.

Primary hyperlipidemia (including heterozygous familial hypercholesterolemia)
Repatha is indicated as an adjunct to diet, alone or in combination with other lipid-lowering therapies (e.g., statins, ezetimibe) for the treatment of adults with primary hyperlipidemia (including heterozygous familial hypercholesterolemia) or to reduce low-density lipoprotein cholesterol (LDL-C).

Homozygous familial hypercholesterolemia (HoFH)
Repatha is indicated as an adjunct to diet and other LDL-lowering therapies (e.g., statins, ezetimibe, LDL apheresis) in patients with homozygous familial hypercholesterolemia (HoFH) who require additional lowering of LDL-C.

CRITERIA FOR APPROVAL

1. Is the requested drug being requested to reduce the risk of myocardial infarction, stroke, or coronary revascularization in a patient with established cardiovascular disease? [If yes, no further questions.]
   - Yes
   - No

2. Does the patient have a diagnosis of primary hyperlipidemia (including heterozygous familial hypercholesterolemia)? [If yes, no further questions.]
   - Yes
   - No

3. Does the patient have a diagnosis of homozygous familial hypercholesterolemia?
   - Yes
   - No

Guidelines for Approval

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Mapping Instructions

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RATIONALE
These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to ensure that patients follow selection elements noted in labeling and/or practice guidelines in order to decrease the potential for inappropriate utilization.

REFERENCES

DOCUMENT HISTORY
Written: Specialty Clinical Development (HY) 08/2015
Revised: HY/DK 10/2015, DK 02/2016, 08/2016 (updates per Praluent CMS feedback), TS 04/2017, LP 01/2018 (label update), 02/2018, 05/2018 (P&T), JC 04/2019 (MA feedback), JC 06/2019 (CMS)
Reviewed: CDPR/AD/ADA 08/2015, 11/2015, ADA 03/2016, SD 10/2016, SD 04/2017, ME 02/2018, ABM 03/2018
External Review: 08/2015, 04/2016, 05/2017, 03/2018
ENHANCED SPECIALTY GUIDELINE MANAGEMENT

REPATHA (evolocumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Repatha is indicated to reduce the risk of myocardial infarction, stroke, and coronary revascularization in adults with established cardiovascular disease.

B. Repatha is indicated as an adjunct to diet, alone or in combination with other lipid-lowering therapies (e.g., statins, ezetimibe), for the treatment of adults with primary hyperlipidemia (including heterozygous familial hypercholesterolemia) to reduce low-density lipoprotein cholesterol.

C. Repatha is indicated as an adjunct to diet and other LDL-lowering therapies (e.g., statins, ezetimibe, LDL apheresis) for the treatment of patients with homozygous familial hypercholesterolemia (HoFH) who require additional lowering of LDL-C.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review:

A. Current LDL-C level for both initial requests and continuation requests. The level must be dated within the six months preceding the authorization request.

B. Untreated (before any lipid lowering therapy) LDL-C level if requesting Repatha to treat primary hyperlipidemia, heterozygous or homozygous familial hypercholesterolemia.

C. Chart notes confirming clinical atherosclerotic cardiovascular disease (ASCVD) if requesting Repatha to treat clinical ASCVD.

D. If patient has contraindication or intolerance to statins, chart notes confirming the contraindication or intolerance. (See Appendix B and C).

III. CRITERIA FOR INITIAL APPROVAL

A. Clinical atherosclerotic cardiovascular disease (ASCVD)

Authorization of 6 months may be granted for treatment of clinical atherosclerotic cardiovascular disease when all of the following criteria are met:

1. Member has a history of clinical ASCVD (See Appendix A).

2. Member meets at least one of the following requirements:

   a. Member has a current LDL-C level ≥ 70 mg/dL after at least three months of treatment with a high-intensity statin dose in combination with ezetimibe. If the member is unable to tolerate a high-intensity statin dose, a moderate-intensity statin dose may be used.

   b. Member has a current LDL-C level ≥ 70 mg/dL with contraindication or intolerance to statins (See Appendix B and C).
B. Primary hyperlipidemia including heterozygous familial hypercholesterolemia (HeFH)

Authorization of 6 months may be granted for treatment of primary hyperlipidemia including heterozygous familial hypercholesterolemia (HeFH) when both of the following criteria are met:

1. Member had an untreated (before any lipid lowering therapy) LDL-C level \( \geq 190 \text{ mg/dL} \) in the absence of a secondary cause.

2. Member meets one of the following criteria:
   a. Member has current LDL-C level \( \geq 100 \text{ mg/dL} \) after at least three months of treatment with a high-intensity statin dose in combination with ezetimibe. If the member is unable to tolerate a high-intensity statin dose, a moderate-intensity statin dose may be used.
   b. Member has current LDL-C level \( \geq 100 \text{ mg/dL} \) with a contraindication or intolerance to statins (See Appendix B and C).

C. Homozygous familial hypercholesterolemia (HoFH)

Authorization of 6 months may be granted for treatment of homozygous familial hypercholesterolemia when both of the following criteria are met:

1. Member had an untreated (before any lipid lowering therapy) LDL-C level \( \geq 190 \text{ mg/dL} \) in the absence of a secondary cause.

2. Member meets one of the following criteria:
   a. Member has a current LDL-C level \( \geq 100 \text{ mg/dL} \) after at least three months of treatment with a high-intensity statin dose in combination with ezetimibe. If the member is unable to tolerate a high-intensity statin dose, a moderate-intensity statin dose may be used.
   b. Member has a current LDL-C level \( \geq 100 \text{ mg/dL} \) with a contraindication or intolerance to statins (See Appendix B and C).
   c. Member has received Juxtapid or Kynamro.
   d. Member has been treated regularly with lipid apheresis.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members who achieve or maintain an LDL-C reduction (e.g., LDL-C is now at goal, robust lowering of LDL-C).

V. APPENDICES

APPENDIX A. Clinical ASCVD
- Acute coronary syndromes
- Myocardial infarction
- Stable or unstable angina
- Coronary or other arterial revascularization procedure (e.g., percutaneous coronary angioplasty [PTCA], coronary artery bypass graft [CABG] surgery)
- Stroke of presumed atherosclerotic origin
- Transient ischemic attack (TIA)
- Non-cardiac peripheral arterial disease of presumed atherosclerotic origin (e.g., carotid artery stenosis)
- Obstructive coronary artery disease (defined as fifty percent or greater stenosis on cardiac computed tomography angiogram or catheterization)

APPENDIX B. Statin-associated muscle symptoms (SAMS) and statin re-challenge
- Score of 7 or higher on the Statin-Associated Muscle Symptom Clinical Index (SAMS-CI)
- Statin-associated elevation in creatine kinase (CK) level \( \geq 10 \text{ times upper limit of normal (ULN)} \)
NOTE: Statin re-challenge is NOT required for members who have experienced an elevation of CK level ≥10 times ULN after receiving lipid-lowering therapy (LLT) with a statin.

APPENDIX C. Contraindications to statins
- Active liver disease, including unexplained persistent elevations in hepatic transaminase levels (e.g., alanine transaminase (ALT) level ≥ 3 times ULN)
- Pregnancy or planned pregnancy
- Breastfeeding

VI. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

REVlimid (lenalidomide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Multiple myeloma in combination with dexamethasone.
   2. Multiple myeloma, as maintenance following autologous hematopoietic stem cell transplantation (auto-HSCT).
   3. Transfusion-dependent anemia due to low- or intermediate-1-risk myelodysplastic syndromes associated with a deletion 5q cytogenetic abnormality with or without additional cytogenetic abnormalities.
   4. Mantle cell lymphoma whose disease has relapsed or progressed after two prior therapies, one of which included bortezomib.

B. Compendial Uses
   1. Multiple myeloma
   2. Systemic light chain amyloidosis
   3. Classical Hodgkin lymphoma
   4. Myelodysplastic syndrome without the 5q deletion cytogenetic abnormality
   5. Myelofibrosis-associated anemia
   6. POEMS Syndrome
   7. Non-Hodgkin lymphoma (NHL) with any of the following subtypes:
      a. AIDS-related diffuse large B-cell lymphoma
      b. Primary central nervous system (CNS) lymphoma
      c. Monomorphic post-transplant lymphoproliferative disorder
      d. Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)
      e. Diffuse large B-cell lymphoma
      f. Follicular lymphoma
      g. Nongastric/Gastric mucosa associated lymphoid tissue (MALT) lymphoma
      h. Primary cutaneous B-cell lymphoma
      i. Nodal/splenic marginal zone lymphoma
      j. Multicentric Castleman’s disease
      k. Adult T-cell leukemia/lymphoma
      l. Mycosis fungoides (MF)/Sezary syndrome (SS)
      m. Angioimmunoblastic T-cell lymphoma (AITL)
      n. Peripheral T-cell lymphoma not otherwise specified (PTCL NOS)
      o. Enteropathy-associated T-cell lymphoma
      p. Monomorphic epitheliotropic intestinal T-cell lymphoma
      q. Nodal peripheral T-cell lymphoma
      r. Follicular T-cell lymphoma
      s. Primary cutaneous anaplastic large cell lymphoma (ALCL)

All other indications are considered experimental/investigational and are not covered benefits.
II. CRITERIA FOR INITIAL APPROVAL

A. Multiple myeloma
   Authorization of 12 months may be granted for treatment of multiple myeloma.

B. Non-Hodgkin lymphoma (NHL)
   Authorization of 12 months may be granted for treatment of NHL with any of the following subtypes:
   1. AIDS-related diffuse large B-cell lymphoma
   2. Primary central nervous system (CNS) lymphoma
   3. Monomorphic post-transplant lymphoproliferative disorder
   4. Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)
   5. Diffuse large B-cell lymphoma
   6. Follicular lymphoma
   7. Mantle cell lymphoma
   8. Nongastric/Gastric MALT lymphoma
   9. Primary cutaneous B-cell lymphoma
   10. Nodal/splenic marginal zone lymphoma
   11. Multicentric Castleman’s disease
   12. Primary cutaneous anaplastic large cell lymphoma (ALCL) (monotherapy only)
   13. Adult T-cell leukemia/lymphoma
   14. Mycosis fungoides (MF)/Sezary syndrome (SS)
   15. Angioimmunoblastic T-cell lymphoma (AITL)
   16. Peripheral T-cell lymphoma not otherwise specified (PTCL NOS)
   17. Enteropathy-associated T-cell lymphoma
   18. Mantle cell lymphoma
   19. Diffuse large B-cell lymphoma
   20. Follicular lymphoma
   21. Nodular peripheral T-cell lymphoma
   22. Follicular T-cell lymphoma

C. Myelodysplastic syndrome
   Authorization of 12 months may be granted for treatment of low- to intermediate-1 risk myelodysplastic syndrome for those with symptomatic anemia.

D. Myelofibrosis-associated anemia
   Authorization of 12 months may be granted for treatment of myelofibrosis-associated anemia.

E. Systemic light chain amyloidosis
   Authorization of 12 months may be granted for treatment of systemic light chain amyloidosis.

F. Classical Hodgkin lymphoma
   Authorization of 12 months may be granted for treatment of classical Hodgkin lymphoma.

G. POEMS Syndrome
   Authorization of 12 months may be granted for treatment of POEMS syndrome.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

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ENHANCED SPECIALTY GUIDELINE MANAGEMENT

DMARD Combination for the Treatment of Rheumatoid Arthritis

Actemra, Cimzia, Enbrel, Humira, Inflectra, Kevzara, Kineret, Olumiant, Orencia
Remicade, Renflexis, Simponi, Simponi Aria, Xeljanz, Xeljanz XR

PROGRAM RATIONALE: The intent of the criteria is to provide coverage for branded biologic disease modifying antirheumatic drugs (DMARDs) for members who have maximized the use of non-biologic generic DMARDs for the treatment of rheumatoid arthritis. For this program, all branded specialty medications approved for the treatment of rheumatoid arthritis (Actemra, Cimzia, Enbrel, Humira, Inflectra, Kevzara, Kineret, Olumiant, Orencia, Remicade, Renflexis, Simponi, Simponi Aria, Xeljanz, Xeljanz XR) are targeted.

STEP THERAPY CRITERIA
If the member has inadequate response, intolerance or contraindication to treatment with generic DMARD medications, the requested branded medication will be approved, provided that the member has met all criteria for approval on all programs implemented for the client. These step therapy criteria only apply to adult members who have not received treatment with any branded biologic or targeted synthetic DMARD for the treatment of rheumatoid arthritis.

Coverage for a requested branded biologic or targeted synthetic disease modifying antirheumatic drug (DMARD) is provided when the member meets one of the following (criteria set A or B):

A. Member has previously received a branded biologic or targeted synthetic DMARD for rheumatoid arthritis (RA)

B. Member has not previously received a branded biologic or targeted synthetic DMARD for RA and meets one of the following (criteria set 1 or 2):

1. Member has failed to achieve a low disease activity after a 3-month trial of a treatment regimen of methotrexate (MTX) at a maximum titrated dose of 20 mg per week and meets any of the following conditions:
   a. Member has had a documented inadequate response with methotrexate in combination with at least one other non-biologic DMARD (i.e., leflunomide, hydroxychloroquine, and/or sulfasalazine) after a 3-month trial at a maximum tolerated dose
   b. Member has experienced a documented intolerable adverse event or has a documented contraindication to leflunomide, hydroxychloroquine, and/or sulfasalazine (see Appendix B)
   c. Member has moderate to high disease activity

2. Member has experienced a documented intolerable adverse event or has a documented contraindication to MTX (see Appendix A) and meets any of the following conditions:
   a. Member has had a documented inadequate response with another non-biologic DMARD (i.e., leflunomide, hydroxychloroquine, and/or sulfasalazine) alone or in combination after a 3-month trial at a maximum tolerated dose(s)
   b. Member has experienced an intolerable adverse event or has a contraindication to leflunomide, hydroxychloroquine, and/or sulfasalazine (see Appendix B)
   c. Member has moderate to high disease activity
APPENDICES

Appendix A: Examples of contraindications to methotrexate

- Alcoholism, alcoholic liver disease or other chronic liver disease
- Blood dyscrasias (e.g. bone marrow hypoplasia, leukopenia, thrombocytopenia, or significant anemia)
- Breastfeeding
- Elevated liver transaminases
- History of intolerance or intolerable adverse event
- Hypersensitivity
- Interstitial pneumonitis or clinically significant pulmonary fibrosis
- Myelodysplasia
- Pregnancy
- Renal impairment
- Significant drug interaction

Appendix B: Examples of contraindications to leflunomide, hydroxychloroquine, and/or sulfasalazine

- Alcoholism, alcoholic liver disease or other chronic liver disease
- Blood dyscrasias (e.g. bone marrow hypoplasia, leukopenia, thrombocytopenia, or significant anemia)
- Breastfeeding
- Chronic liver disease
- Elevated liver transaminases
- Hypersensitivity
- Intestinal or urinary obstruction
- History of intolerance or intolerable adverse event
- Porphyria
- Pregnancy
- Presence of retinal or visual field changes attributable to any 4-aminoquinoline compound

Note: Submission of chart notes detailing the outcomes of treatment, intolerable adverse event(s) experienced, contraindication(s), or exclusion(s) to treatment with prerequisite product(s) is required (where applicable).

REFERENCES


SPECIALTYGUIDELINE MANAGEMENT

RIBAVIRIN PRODUCTS
(COPEGUS, MODERIBA, REBETOL, RIBASPHERE, RIBASPHERE RIBAPAK, RIBATAB, ribavirin capsules and tablets)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Copegus
Copegus is indicated for the treatment of chronic hepatitis C (CHC) virus infection in combination with Pegasys in patients 5 years of age and older with compensated liver disease not previously treated with interferon alpha, and in adult CHC patients coinfected with HIV.

Moderiba
Moderiba is indicated for the treatment of chronic hepatitis C (CHC) virus infection in combination with peginterferon alfa-2a in patients 5 years of age and older with compensated liver disease not previously treated with interferon alpha, and in adult CHC patients coinfected with HIV.

Rebetol
Rebetol is indicated in combination with interferon alfa-2b (pegylated and nonpegylated) for the treatment of chronic hepatitis C (CHC) in patients 3 years of age and older with compensated liver disease.

Ribosphere/RibaPak
Ribosphere is indicated for the treatment of chronic hepatitis C (CHC) virus infection in combination with peginterferon alfa-2a in patients 5 years of age and older with compensated liver disease not previously treated with interferon alpha, and in adult CHC patients coinfected with HIV.

All other indications are considered experimental/investigational and are not a covered benefit.

II. EXCLUSIONS

Exclusions to other antiviral drugs being used in combination with the requested drug apply. Refer to the SGM policy for each drug in the treatment regimen for applicable exclusions.

III. CRITERIA FOR APPROVAL

Chronic hepatitis C virus (HCV) infection
Refer to the SGM of requested regimen for the specific criteria for approval and approval durations.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

RINVOQ (upadacitinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to methotrexate.

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Moderately to severely active rheumatoid arthritis (RA)
A. Authorization of 12 months may be granted for members who have previously received a biologic or targeted synthetic DMARD (e.g., Xeljanz, Olumiant) indicated for moderately to severely active rheumatoid arthritis.

B. Authorization of 12 months may be granted for treatment of moderately to severely active RA when any of the following criteria is met:
   1. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
   2. Member has an intolerance or contraindication to methotrexate (See Appendix A).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who are using Rinvoq for an indication outlined in section II and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic DMARDs or targeted synthetic DMARDs (e.g., Xeljanz), and repeated yearly for members with risk factors** for TB that are continuing therapy with biologics.

* If the screening testing for TB is positive, there must be documentation of further testing to confirm there is no active disease. Do not administer upadacitinib to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of upadacitinib.
** Risk factors for TB include: Persons with close contact to people with infectious TB disease; persons who have recently immigrated from areas of the world with high rates of TB (e.g., Africa, Asia, Eastern Europe, Latin America, Russia); children less than 5 years of age who have a positive TB test; groups with high rates of TB transmission (e.g., homeless persons, injection drug users, persons with HIV infection); persons who work or reside with people who are at an increased risk for active TB (e.g., hospitals, long-term care facilities, correctional facilities, homeless shelters).

For all indications: Member cannot use Rinvoq concomitantly with any biologic DMARD, targeted synthetic DMARD, or potent immunosuppressants such as azathioprine or cyclosporine.

V. APPENDICES

**Appendix A: Examples of Contraindications to Methotrexate**
1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy
10. Renal impairment
11. Significant drug interaction

VI. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

RITUXAN HYCELA (rituximab and hyaluronidase human)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Adult patients with follicular lymphoma (FL):
   i. Relapsed or refractory, follicular lymphoma as a single agent
   ii. Previously untreated follicular lymphoma in combination with first line chemotherapy and, in patients achieving a complete or partial response to rituximab in combination with chemotherapy, as single-agent maintenance therapy
   iii. Non-progressing (including stable disease), follicular lymphoma as a single agent after first-line CVP (cyclophosphamide, vincristine, and prednisone) chemotherapy

2. Adult patients with previously untreated diffuse large B-cell lymphoma (DLBCL) in combination with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) or other anthracycline-based chemotherapy regimens

3. Adult patients with previously untreated and previously treated chronic lymphocytic leukemia (CLL), in combination with fludarabine and cyclophosphamide (FC)

Limitations of Use:

Initiate treatment with Rituxan Hycela only after patients have received at least one full dose of a rituximab product by intravenous infusion.

Rituxan Hycela is not indicated for the treatment of non-malignant conditions.

B. Compendial Uses

1. Acquired immune deficiency syndrome (AIDS)-related B-cell lymphoma
2. Burkitt lymphoma
3. Castleman’s disease (CD)
4. High-grade B-cell lymphoma
5. Gastric mucosa-associated lymphoid tissue (MALT) lymphoma
6. Mantle cell lymphoma
7. Nodal marginal zone lymphoma
8. Nongastric MALT lymphoma
9. Primary cutaneous B-cell lymphoma (e.g., cutaneous marginal zone lymphoma or cutaneous follicle center lymphomas)
10. Post-transplant lymphoproliferative disorder (PTLD)
11. Small lymphocytic lymphoma (SLL)
12. Splenic marginal zone lymphoma

All other indications are considered experimental/investigational and are not a covered benefit.
II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Testing or analysis confirming CD20 protein on the surface of the B-cell.

III. CRITERIA FOR INITIAL APPROVAL

Prior to initiating therapy, all members must receive at least one full dose of a rituximab product by intravenous infusion without experiencing severe adverse reactions.

A. Follicular lymphoma (FL)
   Authorization of 12 months may be granted for treatment of CD20 positive FL.

B. Diffuse large B-cell lymphoma (DLBCL)
   Authorization of 12 months may be granted for treatment of CD20 positive DLBCL.

C. Chronic lymphocytic leukemia (CLL)/ Small lymphocytic lymphoma (SLL)
   Authorization of 12 months may be granted for treatment of CD20 positive CLL or SLL.

D. B-cell lymphomas
   Authorization of 12 months may be granted for treatment of any of the following oncologic disorders that are CD20-positive as confirmed by testing or analysis:
   1. Acquired immune deficiency syndrome (AIDS)-related B-cell lymphoma
   2. Burkitt lymphoma
   3. Castleman’s disease (CD)
   4. Gastric MALT lymphoma
   5. High-grade B-cell lymphoma
   6. Mantle cell lymphoma
   7. Nodal marginal zone lymphoma
   8. Nongastric MALT lymphoma
   9. Primary cutaneous B-cell lymphoma (e.g., cutaneous marginal zone lymphoma or cutaneous follicle center lymphomas)
   10. Post-transplant lymphoproliferative disorder (PTLD)
   11. Splenic marginal zone lymphoma

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced an unacceptable toxicity.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

RITUXAN (rituximab)
TRUXIMA (rituximab-abbs)
RUXIENCE (rituximab-pvvr)

Treatment of Hematologic and Oncologic Conditions

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Non-Hodgkin’s lymphoma (NHL) in adult patients with:
      a. Relapsed or refractory, low-grade or follicular, CD20-positive, B-cell NHL as a single agent
      b. Previously untreated follicular, CD20-positive, B-cell NHL in combination with first line chemotherapy and, in patients achieving a complete or partial response to a rituximab product in combination with chemotherapy, as single-agent maintenance therapy
      c. Non-progressing (including stable disease), low-grade, CD20-positive, B-cell NHL as a single agent after first-line CVP (cyclophosphamide, vincristine, and prednisone) chemotherapy
      d. Previously untreated diffuse large B-cell, CD20-positive NHL in combination with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) or other anthracycline-based chemotherapy regimens
   2. Chronic lymphocytic leukemia (CLL), in combination with fludarabine and cyclophosphamide (FC), for the treatment of adult patients with previously untreated and previously treated CD20-positive CLL.
   3. Granulomatosis with polyangiitis (Wegener’s Granulomatosis) and microscopic polyangiitis (MPA) in adult patients (Not addressed in this policy – Refer to Rituxan-RA+Other SGM)
   4. Moderately to severely active rheumatoid arthritis in adult patients who have had an inadequate response to one or more TNF antagonist therapies (Not addressed in this policy – Refer to Rituxan-RA+Other SGM)
   5. Moderate to severe pemphigus vulgaris in adult patients (Not addressed in this policy – Refer to Rituxan-RA+Other SGM)

B. Compendial Uses
   1. Sjögren’s syndrome (Not addressed in this policy – Refer to Rituxan-RA+Other SGM)
   2. Multiple sclerosis (Not addressed in this policy – Refer to Rituxan-RA+Other SGM)
   3. Neuromyelitis optica (Devic disease) (Not addressed in this policy – Refer to Rituxan-RA+Other SGM)
   4. Idiopathic inflammatory myopathy, refractory (Not addressed in this policy – Refer to Rituxan-RA+Other SGM)
   5. Non-Hodgkin’s lymphoma
      a. Small lymphocytic lymphoma (SLL)
      b. Mantle cell lymphoma
      c. Marginal zone lymphomas (nodal, splenic, gastric MALT, nongastric MALT)
      d. Burkitt lymphoma
      e. Primary cutaneous B-cell lymphoma
f. High-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 (double/triple hit lymphoma)
g. High-grade B-cell lymphoma, not otherwise specified
h. Castleman’s disease
i. Acquired immunodeficiency syndrome (AIDS)-related B-cell lymphoma
j. Hairy cell leukemia
k. Post-transplant lymphoproliferative disorder (PTLD)
l. B-cell lymphoblastic lymphoma
6. Relapsed/refractory immune or idiopathic thrombocytopenic purpura (ITP)
7. Autoimmune hemolytic anemia
8. Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma (LPL)
9. Thrombotic thrombocytopenic purpura
10. Myasthenia gravis, refractory
11. Hodgkin’s lymphoma, nodular lymphocyte-predominant
12. Chronic graft-versus-host disease (GVHD)
13. Central nervous system (CNS) cancers
   a. Leptomeningeal metastases from lymphomas
   b. Primary CNS lymphoma
14. B-cell acute lymphoblastic leukemia (ALL)
15. Prevention of Epstein-Barr virus (EBV)-related PTLD in high risk patients
16. Immune checkpoint inhibitor-related toxicities

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Testing or analysis confirming CD20 protein on the surface of the B-cell (if applicable)

III. CRITERIA FOR INITIAL APPROVAL

A. Oncologic indications

Authorization of 12 months may be granted for treatment of any of the following oncologic disorders that are CD20-positive as confirmed by testing or analysis:

1. Non-Hodgkin’s lymphoma (NHL) with any of the following subtypes:
   a. Diffuse large B-cell lymphoma
   b. High-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 (double/triple hit lymphoma)
   c. High-grade B-cell lymphoma, not otherwise specified
   d. Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)
   e. Follicular lymphoma
   f. Mantle cell lymphoma
   g. Marginal zone lymphomas (nodal, splenic, gastric/non-gastric MALT)
   h. Burkitt lymphoma
   i. Primary cutaneous B-cell lymphoma
   j. Castleman’s disease
   k. AIDS-related B-cell lymphoma
   l. Hairy cell leukemia
   m. Post-transplant lymphoproliferative disorder (PTLD)
n. B-cell lymphoblastic lymphoma
2. Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma (LPL)
3. Hodgkin’s lymphoma, nodular lymphocyte-predominant
4. Central nervous system (CNS) cancers with either of the following:
   a. Leptomeningeal metastases from lymphomas
   b. Primary CNS lymphoma
5. B-cell acute lymphoblastic leukemia (ALL)

B. Hematologic indications
Authorization of 12 months may be granted for treatment of any of the following indications:
1. Refractory immune or idiopathic thrombocytopenic purpura (ITP)
2. Autoimmune hemolytic anemia
3. Thrombotic thrombocytopenic purpura
4. Chronic graft-versus-host disease (GVHD)
5. Prevention of Epstein-Barr virus (EBV)-related PTLD

C. Myasthenia gravis
Authorization of 12 months may be granted for treatment of refractory myasthenia gravis.

D. Immune checkpoint inhibitor-related toxicities
Authorization of 3 months may be granted for treatment of immune checkpoint inhibitor-related toxicities.

IV. CONTINUATION OF THERAPY
For oncologic indications: Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an oncologic indication listed in Section III A. who have not experienced an unacceptable toxicity.

For immune checkpoint inhibitor-related toxicities: Authorization of 3 months may be granted for continued treatment in members requesting reauthorization for treatment of immune checkpoint inhibitor-related toxicities who are experiencing benefit from therapy.

For all other indications: Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III B.-C. who are experiencing benefit from therapy.

V. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

RITUXAN (rituximab)
TRUXIMA (rituximab-abbs)
RUXIENCE (rituximab-pvvr)

Treatment of Rheumatoid Arthritis and Other Conditions

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Moderately to severely active rheumatoid arthritis (RA)
      In combination with methotrexate in patients who have inadequate response to one or more TNF antagonist therapies
   2. Granulomatosis with Polyangiitis (GPA) (Wegener’s Granulomatosis) and Microscopic Polyangiitis (MPA)
      In combination with glucocorticoids
   3. Moderate to severe pemphigus vulgaris
   4. Other FDA-approved indications (not addressed in this policy – Refer to Rituxan–Oncology SGM)
      a. Non-Hodgkin’s lymphoma (NHL)
      b. Chronic lymphocytic leukemia (CLL)

B. Compendial Uses
   1. Sjögren’s syndrome
   2. Multiple sclerosis, relapsing remitting
   3. Neuromyelitis optica (Devic disease)
   4. Idiopathic inflammatory myopathy, refractory
   5. For other compendial uses, refer to Rituxan–Oncology SGM

All other indications are considered experimental/investigational and are not a covered benefit.

II. EXCLUSIONS

Coverage will not be provided for requests for the treatment of rheumatoid arthritis when planned date of administration is less than 16 weeks since date of last dose received.

III. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active rheumatoid arthritis (RA)
   1. Authorization of 24 months may be granted to members who have previously received any biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) indicated for the treatment of moderately to severely active rheumatoid arthritis OR have received at least two full doses of Rituxan for the
treatment of RA, where the most recent dose was given within 6 months of the request. Rituxan must be prescribed in combination with methotrexate (MTX) unless the member has a contraindication or intolerance to MTX (see Appendix A).

2. Authorization of 24 months may be granted for treatment of moderately to severely active RA when all of the following criteria are met:
   a. Member is prescribed Rituxan in combination with MTX or has a contraindication or intolerance to MTX.
   b. Member meets any of the following criteria:
      i. Member has experienced an inadequate response to at least a 3-month trial of MTX despite adequate dosing (i.e., titrated to 20 mg/week)
      ii. Member has an intolerance or contraindication to MTX (see Appendix A)

B. Granulomatosis with polyangiitis (GPA) (Wegener’s granulomatosis) and microscopic polyangiitis (MPA)
   Authorization of 24 months may be granted for treatment of GPA or MPA.

C. Sjögren’s syndrome
   Authorization of 24 months may be granted for treatment of Sjögren’s syndrome.

D. Multiple sclerosis
   Authorization of 24 months may be granted for treatment of multiple sclerosis (MS) when both of the following criteria are met:
   1. Member has a diagnosis of relapsing remitting MS
   2. Member has had an inadequate response to two or more disease-modifying drugs indicated for MS despite adequate duration of treatment (see Appendix B)

E. Neuromyelitis optica
   Authorization of 24 months may be granted for treatment of neuromyelitis optica.

F. Idiopathic inflammatory myopathy
   Authorization of 24 months may be granted for treatment of refractory polymyositis or dermatomyositis.

G. Pemphigus vulgaris
   Authorization of 24 months may be granted for treatment of moderate to severe pemphigus vulgaris.

IV. CONTINUATION OF THERAPY

A. Rheumatoid arthritis
   Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least two doses of therapy with rituximab as evidenced by low disease activity or improvement in signs and symptoms of the condition.

B. Other indications
   Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria.

V. APPENDICES
Appendix A: Examples of contraindications to methotrexate
1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy (male or female)
10. Renal impairment
11. Significant drug interaction

Appendix B: Disease-modifying drugs indicated for multiple sclerosis
1. Aubagio (teriflunomide)
2. Avonex (interferon beta-1a)
3. Betaseron (interferon beta-1a)
4. Copaxone/Glatopa (glatiramer acetate)
5. Extavia (interferon beta-1a)
6. Gilenya ( fingolimod)
7. Tecfidera (dimethyl fumarate)
8. Plegridy (peginterferon beta-1a)
9. Rebif (interferon beta-1a)
10. Tysabri (natalizumab)
11. Ocrevus (ocrelizumab)

VI. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

ROZLYTREK (entrectinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Solid tumors
   Rozlytrek is indicated for the treatment of adult and pediatric patients 12 years and older with solid tumors that:
   a. have a neurotrophic receptor tyrosine kinase (NTRK) gene fusion without a known acquired resistance mutation,
   b. are metastatic or where surgical resection is likely to result in severe morbidity, and
   c. have no satisfactory alternative treatments or that have progressed following treatment.

2. Non-small cell lung cancer
   Rozlytrek is indicated for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are ROS1-positive.

All other indications are considered experimental/investigational and are not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: NTRK gene fusion status or ROS1 status (where applicable).

III. CRITERIA FOR INITIAL APPROVAL

A. Solid tumors
   Authorization of 12 months may be granted for treatment of solid tumors when all of the following criteria are met:
   1. The tumors have a NTRK gene fusion without a known acquired resistance mutation, as demonstrated by laboratory testing (e.g., next-generation sequencing [NGS] or fluorescence in situ hybridization [FISH]).
   2. The disease is metastatic or surgical resection is likely to result in severe morbidity.
   3. No satisfactory alternative treatments are available or the disease has progressed following standard systemic treatment for the disease.

B. Non-small cell lung cancer (NSCLC)
   Authorization of 12 months may be granted for treatment of metastatic ROS1-positive NSCLC.
IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication in Section III who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

RUBRACA (rucaparib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
1. Treatment of adult patients with deleterious BRCA mutation (germline and/or somatic) associated epithelial ovarian, fallopian tube, or primary peritoneal cancer who have been treated with two or more chemotherapies.
2. Maintenance treatment for adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Epithelial ovarian, fallopian tube, or primary peritoneal cancer
A. Authorization of 12 months may be granted for treatment of epithelial ovarian, fallopian tube, or primary peritoneal cancer when all of the following criteria are met:
   1. Tumor has deleterious BRCA mutation (germline, somatic, or both) as detected by an FDA-approved companion diagnostic test
   2. Member has received two or more prior chemotherapies
B. Authorization of 12 months may be granted for the maintenance treatment of recurrent disease to members who are in complete or partial response to platinum based chemotherapy

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

RUCONEST (recombinant C1 esterase inhibitor)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Treatment of acute attacks in adults and adolescent patients with hereditary angioedema (HAE)

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Indefinite authorization may be granted for treatment of acute hereditary angioedema attacks when either of the following criteria is met:
A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing.
B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
   1. Member has an F12, angiotropin-1, or plasminogen gene mutation as confirmed by genetic testing, or
   2. Member has a family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES


ENHANCED SPECIALTY GUIDELINE MANAGEMENT

RUCONEST (recombinant C1 esterase inhibitor)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Treatment of acute attacks in adults and adolescent patients with hereditary angioedema (HAE)

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review: C4 levels and C1 inhibitor functional and antigenic protein levels.

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of acute hereditary angioedema attacks when either of the following criteria is met:
A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing.
B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
   1. Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing, or
   2. Member has a family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy when all of the following criteria are met:
A. Member meets all initial authorization criteria.
B. Member has experienced reduction in severity and duration of attacks since starting treatment.

V. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

RUZURGI (amifampridine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

RUZURGI is indicated for the treatment of Lambert-Eaton myasthenic syndrome (LEMS) in patients 6 to less than 17 years of age.

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of either of the following diagnostic tests is necessary to initiate prior authorization review:

A. Neurophysiology studies (e.g., electromyography)
B. Anti-P/Q type voltage-gated calcium channel antibody test

III. EXCLUSIONS

Coverage will not be provided for members with a history of seizures.

IV. CRITERIA FOR INITIAL APPROVAL

Lambert-Eaton myasthenic syndrome

Authorization of 6 months may be granted for treatment of Lambert-Eaton myasthenic syndrome (LEMS) when the diagnosis is confirmed by either of the following:

A. Neurophysiology studies (e.g., electromyography)
B. A positive anti-P/Q type voltage-gated calcium channel antibody test

V. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment of Lambert-Eaton myasthenic syndrome (LEMS) in members requesting reauthorization who meet all initial authorization criteria.

VI. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

RYDAPT (midostaurin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Rydapt is indicated, in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation chemotherapy, for the treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) who are FLT3 mutation-positive, as detected by a FDA approved test.

       Limitations of Use: Rydapt is not indicated as a single-agent induction therapy for the treatment of patients with AML.

   2. Rydapt is indicated for the treatment of adult patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated hematological neoplasm (SM-AHN), or mast cell leukemia (MCL).

B. Compendial Uses
   Relapsed/refractory AML

All other indications are considered experimental/investigational and are not covered benefits.

II. CRITERIA FOR INITIAL APPROVAL

A. Acute Myeloid Leukemia (AML)
   Authorization of 12 months may be granted to adult members for the treatment of FLT3 mutation-positive AML.

B. Aggressive Systemic Mastocytosis (ASM), Systemic Mastocytosis with associated hematological neoplasm (SM-AHN), and Mast Cell Leukemia (MCL)
   Authorization of 12 months may be granted to adult members for the treatment of ASM, SM-AHN, or MCL.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.
IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

SAMSCA (tolvaptan)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Treatment of clinically significant hypervolemic and euvolemic hyponatremia (serum sodium <125 mEq/L or less marked hyponatremia that is symptomatic and has resisted correction with fluid restriction), including patients with heart failure and Syndrome of Inappropriate Antidiuretic Hormone (SIADH)

Important Limitations
Patients requiring intervention to raise serum sodium urgently to prevent or to treat serious neurological symptoms should not be treated with Samsca. It has not been established that raising serum sodium with Samsca provides a symptomatic benefit to patients.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Hypervolemic/Euvolemic Hyponatremia
Authorization of 30 days may be granted for members prescribed Samsca when all of the following criteria are met:
A. Therapy was initiated (or re-initiated) in the hospital, for hypervolemic or euvolemic hyponatremia; and
B. Serum sodium was less than 125 mEq/L or serum sodium was less than 135 mEq/L with symptoms (e.g., nausea, vomiting, headache, lethargy, confusion) at the time of therapy initiation; and
C. The member will not receive Samsca continually for greater than 30 days.

III. REFERENCE

SPECIALTY GUIDELINE MANAGEMENT
SENSIPAR (cinacalcet)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Secondary hyperparathyroidism (HPT) in adult patients with chronic kidney disease (CKD) on dialysis
   2. Hypercalcemia in adult patients with parathyroid carcinoma
   3. Hypercalcemia in adult patients with primary HPT for whom parathyroidectomy would be indicated on the basis of serum calcium levels, but who are unable to undergo parathyroidectomy

B. Compendial Use
   Tertiary hyperparathyroidism in post-kidney transplant patients not receiving dialysis

All other indications are considered experimental/investigational and are not a covered benefit.

II. INITIAL CRITERIA FOR APPROVAL

A. Secondary Hyperparathyroidism with CKD on Dialysis
   Authorization of 12 months may be granted for treatment of secondary hyperparathyroidism in a member with chronic kidney disease on dialysis who has a serum calcium level (corrected for albumin) greater than or equal to 8.4 mg/dL (see Appendix).

B. Primary Hyperparathyroidism
   Authorization of 12 months may be granted for treatment of primary hyperparathyroidism in a member who is not able to undergo parathyroidectomy and has a serum calcium level (corrected for albumin) greater than or equal to 8.4 mg/dL (see Appendix).

C. Tertiary Hyperparathyroidism in Post-Kidney Transplant Patients Not Receiving Dialysis
   Authorization of 12 months may be granted for treatment of tertiary hyperparathyroidism in a member who has had a kidney transplant, is not receiving dialysis, and has a serum calcium level (corrected for albumin) greater than or equal to 8.4 mg/dL (see Appendix).

D. Parathyroid Carcinoma
   Authorization of 12 months may be granted for the treatment of parathyroid carcinoma in a member who has a serum calcium level (corrected for albumin) greater than or equal to 8.4 mg/dL (see Appendix).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when the following criteria are met:
A. Secondary Hyperparathyroidism with CKD on Dialysis
   Member is experiencing benefit from therapy as evidenced by a decrease in intact parathyroid hormone (iPTH) levels from pretreatment baseline.

B. All other indications
   Member is experiencing benefit from therapy (e.g., decreased or normalized corrected serum calcium levels since starting therapy).

IV. APPENDIX
   Corrected calcium = measured total calcium + 0.8(4.0 – serum albumin)

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

SEROSTIM (somatropin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Serostim is indicated for the treatment of HIV patients with wasting or cachexia to increase lean body mass and body weight, and improve physical endurance. Concomitant antiretroviral therapy is necessary.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Treatment of HIV patients with wasting or cachexia to increase lean body mass and body weight, and improve physical endurance.

Authorization of 12 weeks may be granted when all of the following criteria are met:

A. Member is diagnosed with HIV-associated wasting/cachexia
B. Member is currently on antiretroviral therapy
C. Trial with suboptimal response to alternative therapies (See Appendix A) or contraindication or intolerance to alternative therapies
D. BMI was less than 18.5 kg/m² prior to initiating therapy with Serostim (See Appendix B)

III. CONTINUATION OF THERAPY

Treatment of HIV patients with wasting or cachexia to increase lean body mass and body weight, and improve physical endurance.

Authorization of 12 weeks may be granted when all of the following criteria are met:

A. Member is diagnosed with HIV-associated wasting/cachexia
B. Member is currently on antiretroviral therapy
C. Member is currently receiving treatment with Serostim excluding obtainment as samples or via manufacturer’s patient assistance programs
D. Current BMI is less than 27 kg/m² (See Appendix B)

IV. APPENDICES

Appendix A – Alternative therapies for HIV Wasting

- Cyproheptadine
- Marinol (dronabinol)
- Megace (megestrol acetate)
- Testosterone therapy if hypogonadal
Appendix B – Calculation of BMI and IBW

\[
\text{BMI} = \frac{\text{Weight (pounds)} \times 703}{\frac{\text{Height (inches)}^2}{\text{Weight (kg)} \times \frac{\text{Height (m)}^2}{}}}
\]

BMI classification:
- Underweight: < 18.5 kg/m²
- Normal weight: 18.5 – 24.9 kg/m²
- Overweight: 25 – 29.9 kg/m²
- Obesity (class 1): 30 – 34.9 kg/m²
- Obesity (class 2): 35 – 39.9 kg/m²
- Extreme obesity: ≥ 40 kg/m²

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

SIGNIFOR (pasireotide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Signifor is indicated for the treatment of adult patients with Cushing’s disease for whom pituitary surgery is not an option or has not been curative.

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. For initial requests: pretreatment urinary free cortisol level
B. For continuation of therapy: current urinary free cortisol level

III. CRITERIA FOR APPROVAL

Cushing’s syndrome/disease

Authorization of 6 months may be granted for the treatment of Cushing’s disease/syndrome in members who either have had surgery that was not curative OR for members who are not candidates for surgery.

IV. CONTINUATION OF THERAPY

Cushing’s syndrome/disease

Authorization of 12 months for continuation of therapy may be granted if the member has lower urinary free cortisol levels since the start of therapy or has improvement in signs or symptoms of the disease.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

SIGNIFOR LAR (pasireotide injectable suspension)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Treatment of patients with acromegaly who have had an inadequate response to surgery and/or for whom surgery is not an option
2. Treatment of patients with Cushing’s disease for whom pituitary surgery is not an option or has not been curative

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Acromegaly

Authorization of 24 months may be granted for the treatment of acromegaly when all of the following criteria are met:

1. Member has a high pretreatment insulin-like growth factor-1 (IGF-1) level for age and/or gender based on the laboratory reference range.
2. Member had an inadequate or partial response to surgery OR there is a clinical reason why the member has not had surgery.

B. Cushing’s syndrome/disease

Authorization of 12 months may be granted for the treatment of Cushing’s disease/syndrome in members who either have had surgery that was not curative OR the member is not a candidate for surgery.

III. CONTINUATION OF THERAPY

A. Authorization of 24 months may be granted for continuation of therapy for acromegaly when the member’s IGF-1 level has decreased or normalized since initiation of therapy.

B. All members (including new members) requesting authorization for 12 months for continuation of therapy for Cushing’s syndrome/disease must meet ALL initial authorization criteria.

IV. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

Revatio (sildenafil tablets and oral suspension)  
sildenafil tablets (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Sildenafil/Revatio is indicated for the treatment of pulmonary arterial hypertension (World Health Organization [WHO] Group 1) in adults to improve exercise ability and delay clinical worsening.

Limitation of use: Adding sildenafil to bosentan therapy does not result in any beneficial effect on exercise capacity.

B. Compendial Use

Secondary Raynaud’s phenomenon (Tablets only)

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Pulmonary Arterial Hypertension

Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:

1. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
2. PAH was confirmed by either criterion (i) or criterion (ii) below:
   i. Pretreatment right heart catheterization with all of the following results:
      a. mPAP ≥ 25 mmHg
      b. PCWP ≤ 15 mmHg
      c. PVR > 3 Wood units
   ii. For infants less than one year of age with any of the following conditions, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed:
      a. Post cardiac surgery
      b. Chronic heart disease
      c. Chronic lung disease associated with prematurity
      d. Congenital diaphragmatic hernia

B. Secondary Raynaud’s Phenomenon

Authorization of 12 months may be granted for treatment of secondary Raynaud’s phenomenon when the patient has had an inadequate response to one of the following medications:

1. Calcium channel blockers
2. Angiotensin receptor blockers
3. Selective serotonin reuptake inhibitors
4. Alpha blockers
5. Topical nitrates

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section II who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. APPENDIX

WHO Classification of Pulmonary Hypertension
1 PAH
1.1 Idiopathic (PAH)
1.2 Heritable PAH
1.3 Drug- and toxin-induced PAH
1.4. PAH associated with:
   1.4.1 Connective tissue diseases
   1.4.2 HIV infection
   1.4.3 Portal hypertension
   1.4.4 Congenital heart diseases
   1.4.5 Schistosomiasis
1.5 PAH long-term responders to calcium channel blockers
1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
1.7 Persistent PH of the newborn syndrome
2 PH due to left heart disease
2.1 PH due to heart failure with preserved LVEF
2.2 PH due to heart failure with reduced LVEF
2.3 Valvular heart disease
2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH
3 PH due to lung diseases and/or hypoxia
3.1 Obstructive lung disease
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders
4 PH due to pulmonary artery obstruction
4.1 Chronic thromboembolic PH
4.2 Other pulmonary artery obstructions
   4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
   4.2.2 Other malignant tumors
   Renal carcinoma
   Uterine carcinoma
   Germ cell tumours of the testis
   Other tumours
4.2.3 Non-malignant tumours
Uterine leiomyoma
4.2.4 Arteritis without connective tissue disease
4.2.5 Congenital pulmonary artery stenosis
4.2.6 Parasites
Hydatidosis

5 PH with unclear and/or multifactorial mechanisms
5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
5.4 Complex congenital heart disease

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

SILIQ (brodalumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy and have failed to respond or have lost response to other systemic therapies.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Moderate to severe plaque psoriasis
A. Authorization of 24 months may be granted for members who are 18 years of age or older who have previously received Siliq, Otezla, or any other biologic DMARD indicated for the treatment of moderate to severe plaque psoriasis.

B. Authorization of 24 months may be granted for treatment of moderate to severe plaque psoriasis for members who are 18 years of age or older when all of the following criteria are met:
   1. At least 5% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
   2. Member meets any of the following criteria:
      a. Member has had an inadequate response or intolerance to pharmacologic treatment with methotrexate, cyclosporine or acitretin.
      b. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine or acitretin (see Appendix).

III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Siliq as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB)

Note: Members who have received Siliq or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) are exempt from requirements related to TB screening in this Policy.
V. APPENDIX

Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin
1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Cannot be used due to risk of treatment-related toxicity
4. Drug interaction
5. Pregnancy or planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VI. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

SIMPONI (golimumab for subcutaneous injection)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Moderately to severely active rheumatoid arthritis (RA) in combination with methotrexate
   2. Active psoriatic arthritis (PsA)
   3. Active ankylosing spondylitis (AS)
   4. Moderately to severely active ulcerative colitis (UC)

B. Compendial Use
   Axial spondyloarthritis

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active rheumatoid arthritis (RA)
   1. Authorization of 24 months may be granted for members who have previously received Simponi or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) indicated for moderately to severely active rheumatoid arthritis. Simponi must be prescribed in combination with methotrexate unless the member has a clinical reason not to use methotrexate (see Appendix A).
   2. Authorization of 24 months may be granted for treatment of moderately to severely active RA when all of the following criteria are met:
      a. Member is prescribed Simponi in combination with methotrexate or has a clinical reason not to use methotrexate.
      b. Member meets any of the following criteria:
         i. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
         ii. Member has an intolerance or contraindication to methotrexate (see Appendix A).

B. Active psoriatic arthritis (PsA)
   Authorization of 24 months may be granted for treatment of active psoriatic arthritis (PsA).

C. Active ankylosing spondylitis (AS) and axial spondyloarthritis
   1. Authorization of 24 months may be granted for members who have previously received Simponi or any other biologic DMARD indicated for active ankylosing spondylitis.
   2. Authorizations of 24 months may be granted for treatment of active ankylosing spondylitis and axial spondyloarthritis when any of the following criteria is met:
a. Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs).

b. Member has an intolerance or contraindication to two or more NSAIDs.

D. Moderately to severly active ulcerative colitis (UC)

1. Authorization of 24 months may be granted for members who have previously received Simponi or any other biologic or targeted synthetic drug (e.g., Xeljanz) indicated for moderately to severely active ulcerative colitis.

2. Authorization of 24 months may be granted for treatment of moderately to severely active UC when any of the following criteria is met:
   a. Member has corticosteroid dependence as evidenced by any of the following:
      i. Member requires continuous corticosteroid therapy.
      ii. Corticosteroids cannot be successfully tapered without a return of ulcerative colitis symptoms.
   b. Member has an inadequate response, intolerance or contraindication to at least one conventional therapy option (see Appendix B).

III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Simponi as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB).

Note: Members who have received Simponi or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) are exempt from requirements related to TB screening in this Policy.

V. APPENDICES

Appendix A: Examples of Contraindications to Methotrexate

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy
10. Renal impairment
11. Significant drug interaction

Appendix B: Examples of Conventional Therapy Options for UC

1. Mild to moderate disease – induction of remission:
   a. Oral mesalamine (e.g., Asacol, Asacol HD, Lialda, Pentasa), balsalazide, olsalazine
   b. Rectal mesalamine (e.g., Canasa, Rowasa)
c. Rectal hydrocortisone (e.g., Colocort, Cortifoam)
d. Alternatives: prednisone, azathioprine, mercaptopurine, sulfasalazine

2. Mild to moderate disease – maintenance of remission:
   a. Oral mesalamine, balsalazide, olsalazine, rectal mesalamine
   b. Alternatives: azathioprine, mercaptopurine, sulfasalazine

3. Severe disease – induction of remission:
   a. Prednisone, hydrocortisone IV, methylprednisolone IV
   b. Alternatives: cyclosporine IV, tacrolimus, sulfasalazine

4. Severe disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: sulfasalazine

5. Pouchitis: Metronidazole, ciprofloxacin
   a. Alternative: rectal mesalamine

VI. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

SIMPONI ARIA (golimumab injection for intravenous use)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
1. Moderately to severely active rheumatoid arthritis (RA) in combination with methotrexate
2. Active psoriatic arthritis (PsA)
3. Active ankylosing spondylitis (AS)

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active rheumatoid arthritis (RA)
   1. Authorization of 24 months may be granted for members who have previously received Simponi Aria or any other biologic DMARD or targeted synthetic DMARD (e.g. Xeljanz) indicated for moderately to severely active rheumatoid arthritis. Simponi Aria must be prescribed in combination with methotrexate unless the member has a clinical reason not to use methotrexate (see Appendix A).

   2. Authorization of 24 months may be granted for treatment of moderately to severely active RA when all of the following criteria are met:
      a. Member is prescribed Simponi Aria in combination with methotrexate or has a clinical reason not to use methotrexate.
      b. Member meets any of the following criteria:
         i. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
         ii. Member has an intolerance or contraindication to methotrexate (See Appendix A).

B. Active psoriatic arthritis (PsA)
   Authorization of 24 months may be granted for treatment of active psoriatic arthritis (PsA).

C. Active ankylosing spondylitis (AS)
   1. Authorization of 24 months may be granted for members who have previously received Simponi Aria or any other biologic DMARD indicated for active ankylosing spondylitis.

   2. Authorization of 24 months may be granted for treatment of active ankylosing spondylitis when any of the following criteria is met:
      a. Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs).
      b. Member has an intolerance or contraindication to two or more NSAIDs.
III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Simponi Aria as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB).

Note: Members who have received Simponi Aria or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) are exempt from requirements related to TB screening in this Policy.

V. APPENDICES

Appendix A: Examples of Contraindications to Methotrexate
1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy
10. Renal impairment
11. Significant drug interaction

Appendix B: Examples of Contraindications to the Use of NSAIDs
1. Allergic-type reaction following aspirin or other NSAID administration
2. Asthma
3. Gastrointestinal bleeding
4. History of intolerance or adverse event
5. Significant drug interaction
6. Urticaria

VI. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

SKYRIZI (risankizumab-rzaa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Moderate to severe plaque psoriasis

A. Authorization of 12 months may be granted for members who are 18 years of age or older who have previously received Skyrizi, Otezla, or any other biologic DMARD indicated for the treatment of moderate to severe plaque psoriasis.

B. Authorization of 12 months may be granted for treatment of moderate to severe plaque psoriasis for members who are 18 years of age or older when all of the following criteria are met:
   1. At least 5% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
   2. Member meets any of the following criteria:
      a. Member has had an inadequate response to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
      b. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine and acitretin (see Appendix).
      c. Member has severe psoriasis that warrants a biologic DMARD as first-line therapy.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 4 months of therapy with Skyrizi as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB).

Note: Members who have received Skyrizi or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) are exempt from requirements related to TB screening in this Policy.
For all indications: Members cannot use Skyrizi concomitantly with any other biologic DMARD or targeted synthetic DMARD.

V. APPENDIX

Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine and Acitretin
1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Cannot be used due to risk of treatment-related toxicity
4. Drug interaction
5. Pregnancy or planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VI. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

SOLIRIS (eculizumab) SGM

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
A. Paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis
B. Atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy
C. Generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AchR) antibody positive
D. Neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive

Limitations of Use: Soliris is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).

All other indications are considered experimental/investigational and are not covered benefits.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review for new requests for treatment of:
A. Atypical hemolytic uremic syndrome: ADAMTS 13 level
B. Paroxysmal nocturnal hemoglobinuria: flow cytometry used to show results of GPI-APs deficiency
C. Generalized myasthenia gravis: anti-acetylcholine receptor (AchR) antibody positive, clinical classification of myasthenia gravis score, MG activities of daily living score, use of IVIG and rituximab, use of two immunosuppressive therapies
D. Neuromyelitis optica spectrum disorder: immunoassay used to confirm anti-aquaporin-4 (AQP4) antibody is present

III. CRITERIA FOR INITIAL APPROVAL

A. Atypical hemolytic uremic syndrome
   Authorization of 6 months may be granted for treatment of atypical hemolytic uremic syndrome not caused by Shiga toxin when all of the following criteria are met:
   1. ADAMTS 13 activity level above 5%
   2. Absence of Shiga toxin

B. Paroxysmal nocturnal hemoglobinuria
   Authorization of 6 months may be granted for treatment of paroxysmal nocturnal hemoglobinuria (PNH) when all of the following criteria are met:
1. The diagnosis of PNH was confirmed by detecting a deficiency of glycosylphosphatidylinositol-anchored proteins (GPI-APs) as demonstrated by either of the following:
   a. At least 5% PNH cells
   b. At least 51% of GPI-anchored protein deficient poly-morphonuclear cells
2. Flow cytometry is used to demonstrate GPI-anchored proteins deficiency

C. Generalized myasthenia gravis (gMG)
Authorization of 6 months may be granted for treatment of generalized myasthenia gravis (gMG) when all of the following criteria are met:
1. Anti-acetylcholine receptor (AChR) antibody positive
2. Myasthenia Gravis Foundation of America (MGFA) clinical classification II to IV
3. MG activities of daily living (MG-ADL) total score ≥6
4. Meets both of the following:
   a. Patient has had an inadequate response to at least two immunosuppressive therapies listed below:
      i. azathioprine
      ii. cyclosporine
      iii. mycophenolate mofetil
      iv. tacrolimus
      v. methotrexate
      vi. cyclophosphamide
   b. Patient has inadequate response to chronic IVIG AND rituximab

D. Neuromyelitis Optica Spectrum Disorder (NMOSD)
Authorization of 6 months may be granted for treatment of neuromyelitis optica spectrum disorder (NMOSD) when all of the following criteria are met:
1. Anti-aquaporin-4 (AQP4) antibody positive
2. Member exhibits one of the following core clinical characteristics of NMOSD:
   a. Optic neuritis
   b. Acute myelitis
   c. Area postrema syndrome (episode of otherwise unexplained hiccups or nausea and vomiting)
   d. Acute brainstem syndrome
   e. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions
   f. Symptomatic cerebral syndrome with NMOSD-typical brain lesions
3. The member will not be treated with rituximab and eculizumab concomitantly

IV. CONTINUATION OF THERAPY

A. Atypical hemolytic uremic syndrome
Authorization of 12 months may be granted to all members requesting continuation of therapy provided they meet all initial authorization criteria and demonstrate a positive response to therapy (e.g., normalization of lactate dehydrogenase (LDH) levels, platelet counts).

B. Paroxysmal nocturnal hemoglobinuria
Authorization of 12 months may be granted to all members requesting continuation of therapy provided they meet all initial authorization criteria and demonstrate a positive response to therapy (e.g., improvement in hemoglobin levels, normalization of LDH levels).

C. Generalized myasthenia gravis (gMG)
Authorization of 12 months may be granted to all members requesting continuation of therapy provided they meet all initial authorization criteria and demonstrate a positive response to therapy
(e.g., improvement in MG-ADL score, changes compared to baseline in Quantitative Myasthenia Gravis (QMG) total score).

D. Neuromyelitis optica spectrum disorder (NMOSD)
Authorization of 12 months may be granted to all members requesting continuation of therapy provided they meet all initial authorization criteria and demonstrate a positive response to therapy (e.g., reduction in number of relapses).

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT
SOLIRIS (eculizumab) ENHANCED SGM

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
A. Paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis
B. Atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy
C. Generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AchR) antibody positive
D. Neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive

Limitations of Use: Soliris is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).

All other indications are considered experimental/investigational and are not covered benefits.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review for new requests for treatment of:
A. Atypical hemolytic uremic syndrome: ADAMTS 13 level
B. Paroxysmal nocturnal hemoglobinuria: flow cytometry used to show results of GPI-APs deficiency
C. Generalized myasthenia gravis: anti-acetylcholine receptor (AchR) antibody positive, clinical classification of myasthenia gravis score, MG activities of daily living score, use of IVIG and rituximab, use of two immunosuppressive therapies
D. Neuromyelitis optica spectrum disorder: immunoassay used to confirm anti-aquaporin-4 (AQP4) antibody is present

III. CRITERIA FOR INITIAL APPROVAL

A. Atypical hemolytic uremic syndrome
Authorization of 6 months may be granted for treatment of atypical hemolytic uremic syndrome not caused by Shiga toxin when all of the following criteria are met:
1. ADAMTS 13 activity level above 5%
2. Absence of Shiga toxin

B. Paroxysmal nocturnal hemoglobinuria
Authorization of 6 months may be granted for treatment of paroxysmal nocturnal hemoglobinuria (PNH) when all of the following criteria are met:
A. The diagnosis of PNH was confirmed by detecting a deficiency of glycosylphosphatidylinositol-anchored proteins (GPI-APs) as demonstrated by either of the following:
   1. At least 5% PNH cells
   2. At least 51% of GPI-anchored protein deficient poly-morphonuclear cells
B. Flow cytometry is used to demonstrate GPI-anchored proteins deficiency

C. Generalized myasthenia gravis (gMG)
   Authorization of 6 months may be granted for treatment of generalized myasthenia gravis (gMG) when all of the following criteria are met:
   1. Anti-acetylcholine receptor (AchR) antibody positive
   2. Myasthenia Gravis Foundation of America (MGFA) clinical classification II to IV
   3. MG activities of daily living (MG-ADL) total score ≥6
   4. Meets both of the following:
      a. Patient has had an inadequate response to at least two immunosuppressive therapies listed below:
         i. azathioprine
         ii. cyclosporine
         iii. mycophenolate mofetil
         iv. tacrolimus
         v. methotrexate
         vi. cyclophosphamide
      b. Member has inadequate response to chronic IVIG AND rituximab

D. Neuromyelitis Optica Spectrum Disorder (NMOSD)
   Authorization of 6 months may be granted for treatment of neuromyelitis optica spectrum disorder (NMOSD) when all of the following criteria are met:
   1. Anti-aquaporin-4 (AQP4) antibody positive
   2. Member exhibits one of the following core clinical characteristics of NMOSD:
      a. Optic neuritis
      b. Acute myelitis
      c. Area postrema syndrome (episode of otherwise unexplained hiccups or nausea and vomiting)
      d. Acute brainstem syndrome
      e. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions
      f. Symptomatic cerebral syndrome with NMOSD-typical brain lesions
   3. The member will not be treated with rituximab and eculizumab concomitantly

IV. CONTINUATION OF THERAPY

A. Atypical hemolytic uremic syndrome
   Authorization of 12 months may be granted to all members requesting continuation of therapy provided they meet all initial authorization criteria and demonstrate a positive response to therapy (e.g., normalization of lactate dehydrogenase (LDH) levels, platelet counts).

B. Paroxysmal nocturnal hemoglobinuria
   Authorization of 12 months may be granted to all members requesting continuation of therapy provided they meet all initial authorization criteria and demonstrate a positive response to therapy (e.g., improvement in hemoglobin levels, normalization of LDH levels).

C. Generalized myasthenia gravis (gMG)
   Authorization of 12 months may be granted to all members requesting continuation of therapy provided they meet all initial authorization criteria and demonstrate a positive response to therapy
(e.g., improvement in MG-ADL scores, changes in baseline in Quantitative Myasthenia Gravis (QMG) total score).

D. Neuromyelitis optica spectrum disorder (NMO SD)

Authorization of 12 months may be granted to all members requesting continuation of therapy provided they meet all initial authorization criteria and demonstrate a positive response to therapy (e.g., reduction in number of relapses).

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

SOMATULINE DEPOT (lanreotide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Somatuline Depot is indicated for the long-term treatment of acromegalic patients who have had an inadequate response to surgery and/or radiotherapy, or for whom surgery and/or radiotherapy is not an option.
   2. Somatuline Depot is indicated for the treatment of patients with unresectable, well- or moderately-differentiated, locally advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NETs) to improve progression-free survival.
   3. Somatuline Depot is indicated for the treatment of adults with carcinoid syndrome; when used, it reduces the frequency of short-acting somatostatin analog rescue therapy.

B. Compendial Uses
   Neuroendocrine tumors (NETs):
   - Tumors of the gastrointestinal (GI) tract, lung, and thymus (carcinoid tumors)
   - Tumors of the pancreas

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Acromegaly
   Authorization of 24 months may be granted for the treatment of acromegaly when all of the following criteria are met:
   1. Member has a high pretreatment insulin-like growth factor-1 (IGF-1) level for age and/or gender based on the laboratory reference range.
   2. Member had an inadequate or partial response to surgery or radiotherapy OR there is a clinical reason why the member has not had surgery or radiotherapy.

B. Neuroendocrine tumors (NETs)
   1. Tumors of the gastrointestinal (GI) tract (carcinoid tumor)
      Authorization of 24 months may be granted for treatment of NETs of the GI tract.
   2. Tumors of the thymus (carcinoid tumor)
      Authorization of 24 months may be granted for treatment of NETs of the thymus.
   3. Tumors of the lung (carcinoid tumor)
      Authorization of 24 months may be granted for treatment of NETs of the lung.
   4. Tumors of the pancreas
      Authorization of 24 months may be granted for treatment of NETs of the pancreas.
C. Carcinoid syndrome
Authorization of 24 months may be granted for treatment of carcinoid syndrome.

III. CONTINUATION OF THERAPY

A. Acromegaly
Authorization of 24 months may be granted for continuation of therapy for acromegaly when the member’s IGF-1 level has decreased or normalized since initiation of therapy.

B. All other indications
Members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

SOMAVER (pegvisomant)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Somavert is indicated for the treatment of acromegaly in patients who have had an inadequate response to surgery or radiation therapy, or for whom these therapies are not appropriate.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 24 months may be granted for the treatment of acromegaly when all of the following criteria are met:

A. Member has a high pretreatment insulin-like growth factor-1 (IGF-1) level for age and/or gender based on the laboratory reference range.

B. Member had an inadequate or partial response to surgery or radiotherapy OR there is a clinical reason why the member has not had surgery or radiotherapy.

III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for continuation of therapy for acromegaly when the member's IGF-1 level has decreased or normalized since initiation of therapy.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

SOVALDI (sofosbuvir)

POLICY

I. INDICATIONS
The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Sovaldi is indicated for the treatment of:
- Adult patients with chronic hepatitis C virus (HCV) infection as a component of a combination antiviral treatment regimen
  - genotype 1 or 4 infection without cirrhosis or with compensated cirrhosis for use in combination with pegylated interferon and ribavirin
  - genotype 2 or 3 infection without cirrhosis or with compensated cirrhosis for use in combination with ribavirin.
- Chronic HCV genotype 2 or 3 infection in pediatric patients 12 years of age and older or weighing at least 35 kg without cirrhosis or with compensated cirrhosis for use in combination with ribavirin.

All other indications are considered experimental/investigational and are not a covered benefit.

Compendial Uses
Chronic hepatitis C genotype 5 or 6 infection (refer to Daklinza SGM)

II. CRITERIA FOR APPROVAL

A. Chronic hepatitis C virus infection, in combination with peginterferon alfa (PEG-IFN) and ribavirin (RBV)
   1. Genotype 1 infection
      Authorization of up to 12 weeks total may be granted for members who are treatment-naïve.
   2. Genotype 4 infection
      Authorization of up to 12 weeks total may be granted for members who are treatment-naïve.

B. Chronic hepatitis C virus infection, in combination with ribavirin
   1. Genotype 1 infection
      Authorization of up to 24 weeks total may be granted for members who have documented interferon (IFN) ineligibility (see Section III).
   2. Genotype 2 infection
      Authorization of up to 12 weeks total may be granted for members who are treatment-naïve or failed prior treatment with PEG-IFN and RBV.
   3. Genotype 3 infection
      Authorization of up to 24 weeks total may be granted for members who are treatment-naïve or failed prior treatment with PEG-IFN and RBV.
   4. Members with hepatocellular carcinoma awaiting liver transplantation
Authorization of up to 48 weeks total or until liver transplantation, whichever occurs first, may be granted for members with genotype 1, 2, 3, or 4 infection and hepatocellular carcinoma who meet the MILAN criteria, defined as the following:

a. Tumor size 5 cm or less in diameter with single hepatocellular carcinomas OR 3 tumor nodules or less, each 3 cm or less in diameter with multiple tumors AND
b. No extrahepatic manifestations of the cancer or evidence of vascular invasion of tumor

C. Chronic hepatitis C virus infection, in combination with Olysio (with or without ribavirin)
Authorization of up to 24 weeks total (as applicable) may be granted for members prescribed Sovaldi in combination with Olysio (with or without ribavirin as applicable) who meet the criteria for approval for the requested regimen. Refer to the Olysio SGM for the specific criteria for approval and approval durations.

D. Chronic hepatitis C virus infection, in combination with Daklinza (with or without ribavirin)
Authorization of up to 24 weeks total (as applicable) may be granted for members prescribed Sovaldi in combination with Daklinza (with or without ribavirin as applicable) who meet the criteria for approval for the requested regimen. Refer to the Daklinza SGM for the specific criteria for approval and approval durations.

E. Chronic hepatitis C virus infection, in combination with Zepatier
Authorization of up to 12 weeks total (as applicable) may be granted for members prescribed Sovaldi in combination with Zepatier who meet the criteria for approval for the requested regimen. Refer to the Zepatier SGM for the specific criteria for approval and approval durations.

F. HCV and HIV coinfection
Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A, B, C, D, or E above are met.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. APPENDIX: INTERFERON INELIGIBILITY
IFN ineligible is defined as one or more of the below:
- Intolerance to IFN
- Autoimmune hepatitis and other autoimmune disorders
- Hypersensitivity to PEG-IFN or any of its components
- Major uncontrolled depressive illness
- A baseline neutrophil count < 1,500/mcL
- A baseline platelet count < 90,000/mcL
- A baseline hemoglobin < 10 g/dL
- History of pre-existing cardiac disease

V. REFERENCES
SPECIALTY POST LIMIT QUANTITY EXCEPTION CRITERIA

I. PROGRAM DESCRIPTION

Coverage is provided for an amount of drug sufficient for most members based on the most common uses of the drug. The submitted prescription is covered up to this standard limit without a review process. In situations where an additional quantity of drug is needed to adequately treat the member, prior authorization is required to determine if clinical exceptions are met.

Coverage for an additional quantity of drug is provided for duration sufficient for most uses (e.g., shorter period of time to accommodate loading doses or dose titration when a member requires additional amounts to adequately treat his/her condition).

In situations where coverage for additional quantities is not approved through the prior authorization process, an appeals process exists to review specific or unique cases where additional drug may be necessary.

II. RATIONALE

The intent of this program is to provide coverage for quantities sufficient for treatment for most members based on the most common uses of the drug. Quantity limits are based on dosage recommendations in product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. In situations where greater amounts of drug are needed, prior authorization criteria allow approval of these quantities based on clinical exceptions such as to accommodate loading doses, compendial supported dosing, drug interactions, or dosing by body weight or body surface area, and to allow for dose adjustments using a particular strength of the drug, as applicable.

III. CRITERIA FOR APPROVAL

The use of medication at the requested quantity is supported by the manufacturer’s prescribing information or dosing guidelines found in the compendia or current literature (e.g., AHFS, Micromedex DrugDex, NCCN compendia, current treatment guidelines) and the member meets the criteria set A, B or C.

A. Authorization for a quantity up to the exception limit may be granted for up to 90 days for initiation of treatment at a higher dose or frequency of administration (e.g., loading dose).

B. Authorization for a quantity up to the exception limit may be granted for up to 6 months when a greater quantity is necessary to adjust the dose using a lower strength due to intolerance to the recommended maintenance dose.

C. Authorization for a quantity up to the exception limit may be granted for up to 12 months or for the remaining duration of any other existing prior authorization (e.g., Specialty Guideline Management) in the following situations:
   1. Member is prescribed a drug dosed by weight or body surface area and requires a greater quantity to achieve the appropriate dose OR
   2. A greater quantity is necessary to accommodate a higher dose following an inadequate response OR
   3. A greater quantity is necessary for a compendial use or an FDA-approved indication OR
   4. A greater quantity is necessary to adjust the dose or frequency of administration to account for a drug interaction.
IV. COVERED QUANTITIES

Coverage is provided without prior authorization up to the standard limits. Coverage of an additional quantity may be provided up to the exception limit with prior authorization. These limits are specified in the Specialty Quantity Limit Program policies for the applicable products.
SPECIALTY QUANTITY LIMIT PROGRAM

VISTOGARD (uridine triacetate)

I. PROGRAM DESCRIPTION

The standard limit is designed to allow a quantity sufficient for the most common uses of the medication. The recommended dosing parameters for all FDA-approved indications fall within the standard limits. Coverage of an additional quantity may be reviewed on a case-by-case basis upon request.

II. COVERED QUANTITIES

<table>
<thead>
<tr>
<th>Medication</th>
<th>Standard Limit</th>
<th>FDA-recommended dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vistogard Pak, oral granules</td>
<td>20 packets per 5 days</td>
<td>Adults: 10 grams (1 packet) orally every 6 hours for 20 doses</td>
</tr>
<tr>
<td>10 gram packet</td>
<td></td>
<td>Pediatric: 6.2 grams/m² of body surface area (not to exceed 10 grams per dose) orally every 6 hours for 20 doses</td>
</tr>
</tbody>
</table>

III. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

SPINRAZA (nusinersen)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Spinraza is indicated for the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients.

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Initiation of therapy:
   1. Deletion or mutation at the SMN1 allele confirmed by genetic testing.
   2. Medical records (e.g., chart notes, laboratory values) of the baseline assessment for at least one of the following assessment tools (based on patient age and motor ability) to establish baseline motor ability:
      i. Hammersmith Infant Neurological Exam Part 2 (HINE-2)
      ii. Hammersmith Functional Motor Scale Expanded (HFMSE)
      iii. Children’s Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND)
B. Continuation of therapy:
   1. Medical records (e.g., chart notes, laboratory values) of the most recent (less than 1 month prior to continuation request) assessment by at least one of the following assessments:
      i. HINE-2
      ii. HFMSE
      iii. CHOP-INTEND
      iv. For members prescribed Spinraza due to clinical worsening after receiving gene therapy: Documentation of the impact of Spinraza therapy (e.g., impact on motor milestones)

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a physician who specializes in treatment of spinal muscular atrophy.

IV. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of SMA when all of the following criteria are met:
A. Member has type 1, type 2 or type 3 SMA.
B. There is genetic documentation of 5q SMA homozygous gene mutation, homozygous gene deletion, or compound heterozygote.
C. The member is 15 years of age or younger at initiation of treatment.
D. Member is not dependent on either of the following:
   1. Invasive ventilation or tracheostomy
   2. Use of non-invasive ventilation for more than 6 hours in a 24-hour period
E. Member meets one of the following criteria:
   1. Member has not previously received gene therapy for SMA, or
   2. Member has previously received gene therapy for SMA and has experienced a worsening in clinical status since receiving gene therapy as demonstrated by a decline of minimally clinical important difference from highest score achieved on one of the following exams (based on member age and motor ability):
      i. HINE-2: Decline of at least 2 points on kicking and 1 point on any other milestone (excluding voluntary grasp)
      ii. HFMSE: Decline of at least 3 points
      iii. CHOP-INTEND: Decline of at least 4 points
F. If the member has not received a loading dose, the loading dose will be dosed at 12 mg (5mL) on Day 0, 14, 28, and 58.

V. CONTINUATION OF THERAPY

Note: Members who were previously established on Spinraza and subsequently administered gene therapy must meet all initial criteria prior to re-starting therapy on Spinraza.

Authorization of 12 months may be granted for continued treatment of SMA when all of the following criteria are met:
A. Member has type 1, type 2 or type 3 SMA.
B. Member is not dependent on either of the following:
   1. Invasive ventilation or tracheostomy
   2. Use of non-invasive ventilation for more than 6 hours in a 24-hour period
C. Submission of medical records (e.g., chart notes, laboratory values) of the most recent (less than 1 month prior to continuation request) assessment documenting a positive clinical response from pretreatment baseline to Spinraza therapy, as demonstrated by at least one of the following assessments:
   1. HINE-2
      i. One of the following:
         a. Member exhibited improvement or maintenance of previous improvement of at least a 2 point (or maximal score) increase in ability to kick; or
         b. Member exhibited improvement or maintenance of previous improvement of at least a 1 point (or maximal score) increase in any other HINE-2 milestone (e.g., head control, rolling, sitting, crawling, standing, or walking) excluding voluntary grasp; and
      ii. One of the following:
         a. Member exhibited improvement or maintenance of previous improvement in more HINE-2 motor milestones than worsening (net positive improvement); or
         b. Member achieved and maintained any new motor milestones when they would otherwise be unexpected to do so (e.g., sit or stand unassisted, walk)
   2. HFMSE
      i. One of the following:
a. Member exhibited improvement or maintenance of previous improvement of at least a 3-point increase in score; or  
b. Member has achieved and maintained any new motor milestone from pretreatment baseline when they would otherwise be unexpected to do so

3. CHOP-INTEND  
i. One of the following: 
   a. Member exhibited improvement or maintenance of previous improvement of at least a 4-point increase in score; or  
   b. Member has achieved and maintained any new motor milestone from pretreatment baseline when they would otherwise be unexpected to do so

4. Member was prescribed Spinraza due to clinical worsening after receiving gene therapy and there is documentation of stabilization or improvement in clinical status with Spinraza therapy (e.g., impact on motor milestones).

D. If member has already received a loading dose, the maintenance dose will not exceed 12 mg (5 mL) every 4 months.

VI. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

SPRAVATO (esketamine) nasal spray

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Spravato is indicated, in conjunction with an oral antidepressant, for the treatment of treatment-resistant depression (TRD) in adults.

Limitations of Use: Spravato is not approved as an anesthetic agent. The safety and effectiveness of Spravato as an anesthetic agent have not been established.

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. For initial requests:
   1. Pretreatment depression severity score(s) from standardized rating scale(s) that reliably measure depressive symptoms (e.g., Beck Depression Scale [BDI], Hamilton Depression Rating Scale [HDRS], Montgomery-Asberg Depression Rating Scale [MADRS], etc.)
   2. Medical records documenting inadequate response with antidepressant and augmentation agents for the current depressive episode (if applicable)

B. For continuation of therapy:
   Current depression severity score(s) from standardized rating scale(s) that reliably measure depressive symptoms

III. EXCLUSION

Coverage will not be provided for members with current or recent history (i.e., within the last 6 months) of moderate or severe substance or alcohol use disorder.

IV. CRITERIA FOR INITIAL APPROVAL

Treatment-resistant depression (TRD)
Authorization of 1 month may be granted for treatment of TRD when all of the following criteria are met:
A. Member has a confirmed diagnosis of severe major depressive disorder (single or recurrent episode), documented by standardized rating scales that reliably measure depressive symptoms (e.g., Beck
B. Diagnosis is verified by a psychiatrist.
C. Member is 18 years of age or older.
D. Requested drug will be administered under the direct supervision of a healthcare provider.
E. Member will be monitored by a health care provider for at least 2 hours after administration.
F. Member meets either of the following criteria:
   1. Member must meet both of the following:
      i. Member has experienced inadequate response during the current depressive episode with two antidepressants (e.g., selective serotonin reuptake inhibitor [SSRI], serotonin-norepinephrine reuptake inhibitor [SNRI], tricyclic antidepressant [TCA], bupropion, mirtazapine) from at least two different classes (different mechanisms of action) at the maximally tolerated labeled dose, each used for at least 8 weeks;
         • Aminoketone (Wellbutrin/SR/XL [bupropion])
         • Monoamine oxidase inhibitors (MAOIs) (e.g., Marplan, Nardil, Parnate, phenelzine, tranylcypromine)
         • Noradrenaline and specific serotoninergic antidepressants (NASSAs) (e.g., amoxapine, maprotiline, mirtazapine/ODT, Oleptro ER, Remeron/Solutab, trazodone)
         • Selective serotonin reuptake inhibitors (SSRIs) (e.g., Celexa, citalopram, escitalopram, fluoxetine, fluvoxamine, Lexapro, Luvox/CR, paroxetine, Paxil/CR, Pexeva, Prozac/Weekly, sertraline, Zoloft)
         • Serotonin-norepinephrine reuptake inhibitors (SNRIs) (e.g., Cymbalta, desvenlafaxine/ER, duloxetine, Effexor/XR, Fetzima, Irenka, Khedezla, Pristiq, venlafaxine/ER)
         • Tricyclic antidepressants (TCAs) (e.g., amitriptyline, desipramine, doxepin, Elavil, imipramine, Norpramin, nortriptyline, Pamelaor, Surmontil, Tofranil, trimipramine)
      ii. Member has experienced an inadequate response with an adequate trial of augmentation therapy OR cognitive behavioral therapy during the current depressive episode
         • Augmentation therapy is defined as:
           o Two antidepressants with different mechanisms of action used concomitantly
           o An antidepressant and a second-generation antipsychotic used concomitantly
           o An antidepressant and lithium used concomitantly
           o An antidepressant and thyroid hormone used concomitantly
           o An antidepressant and buspirone used concomitantly
   2. Member has profound depression and persistent suicidal ideation defined as all of the following:
      i. The prescriber represents that, in the absence of the requested drug, within the next 24 to 48 hours the member will require confinement in an acute care psychiatric institution.
      ii. Member has a depressive episode so acute and so severe that the member is not able to participate in self-care (e.g., washing, eating) and is unable to participate at all in their usual daily activities (e.g., work). Member has persistent thoughts of hopelessness and helplessness as well as anhedonia.
      iii. Member has thoughts of dying and/or self-harm for at least some part of each and every day.
G. Requested drug will be used in combination with an oral antidepressant (e.g., duloxetine, escitalopram, sertraline, venlafaxine).

V. CONTINUATION OF THERAPY

Treatment-resistant depression (TRD)
Authorization of 3 months may be granted for the continuation of treatment of TRD when there is improvement or sustained improvement from baseline in depressive symptoms documented by standardized rating scales that reliably measure depressive symptoms (e.g., Beck Depression Scale [BDI], Hamilton Depression Rating Scale [HDRS], Montgomery-Asberg Depression Rating Scale [MADRS]).
VI. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

SPRYCEL (dasatinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Newly diagnosed adults with Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in chronic phase
2. Adults with chronic, accelerated, or myeloid or lymphoid blast phase Ph+ CML with resistance or intolerance to prior therapy including imatinib
3. Adults with Ph+ acute lymphoblastic leukemia (ALL) with resistance or intolerance to prior therapy
4. Pediatric patients with Ph+ CML in chronic phase
5. Pediatric patients with newly diagnosed Ph+ ALL in combination with chemotherapy

B. Compendial Uses
1. Primary treatment of advanced phase CML (accelerated phase or blast phase)
2. Follow-up therapy for CML patients after hematopoietic stem cell transplant (HSCT)
3. Ph+ ALL as a single agent or in combination with chemotherapy or corticosteroids
4. Induction therapy for Ph+ ALL in adults aged ≥ 65 years
5. Metastatic chondrosarcoma
6. Recurrent chordoma
7. Gastrointestinal stromal tumor (GIST) in patients with PDGFRA D842V mutation and disease progression on imatinib, sunitinib, or regorafenib

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review:
A. Prior to initiation of therapy for treatment of CML or Ph+ ALL: results of cytogenetic and/or molecular testing for detection of the Ph chromosome or the BCR-ABL gene
B. For members requesting initiation of Sprycel therapy for treatment of CML or ALL after experiencing resistance to prior tyrosine kinase inhibitor (TKI) therapy: results of T315I mutation testing

III. CRITERIA FOR INITIAL APPROVAL

A. Chronic Myeloid Leukemia (CML)

Authorization of 6 months may be granted for treatment of CML that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when any of the following criteria are met:
1. Member has not received prior therapy with a TKI (e.g., bosutinib, imatinib, nilotinib, ponatinib)
2. Member experienced toxicity or intolerance to prior therapy with a TKI
3. Member experienced resistance to prior therapy with a TKI and results of mutational testing are negative for T315I mutation
4. Member has received HSCT for CML

B. **Ph+ Acute Lymphoblastic Leukemia (ALL)/Lymphoblastic Lymphoma (LL)**
   Authorization of 12 months may be granted for treatment of Ph+ ALL or LL that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when any of the following criteria are met:
   1. Member has not received prior therapy with a TKI (e.g., bosutinib, imatinib, nilotinib, ponatinib)
   2. Member experienced toxicity or intolerance to prior therapy with a TKI
   3. Member experienced resistance to prior therapy with a TKI and results of mutational testing are negative for T315I mutation

C. **Gastrointestinal Stromal Tumor (GIST)**
   Authorization of 12 months may be granted for treatment of GIST in members with PDGFRA D842V mutation who have experienced disease progression on imatinib, sunitinib, or regorafenib.

D. **Bone Cancer**
   Authorization of 12 months may be granted for treatment of metastatic chondrosarcoma or recurrent chordoma.

IV. **CONTINUATION OF THERAPY**

A. **CML**
   Authorization of 12 months may be granted for continued treatment of CML that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when any of the following criteria are met:
   1. BCR-ABL1 \( \leq 10\% \) for members who have been receiving Sprycel for \( \leq 12 \) months
   2. No evidence of disease progression for members who have been receiving Sprycel for > 12 months
   3. Member has received HSCT

B. **Ph+ ALL/LL**
   Authorization of 12 months may be granted for continued treatment of Ph+ ALL or LL that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing in members who have not experienced disease progression or an unacceptable toxicity.

C. **GIST and Bone Cancer**
   Authorization of 12 months may be granted for continued treatment of GIST, metastatic chondrosarcoma, or recurrent chordoma in members who have not experienced disease progression or an unacceptable toxicity.

V. **REFERENCES**
SPECIALTY GUIDELINE MANAGEMENT

STELARA (ustekinumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
1. Moderate to severe plaque psoriasis (PsO)
2. Active psoriatic arthritis (PsA)
3. Moderately to severely active Crohn’s disease (CD)

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderate to severe plaque psoriasis (PsO)
   1. Authorization of 24 months may be granted for members who are 12 years of age or older who have previously received Stelara, Otezla, or any other biologic DMARD indicated for the treatment of moderate to severe plaque psoriasis.
   2. Authorization of 24 months may be granted for treatment of moderate to severe plaque psoriasis in members who are 12 years of age or older when all of the following criteria are met:
      a. At least 5% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
      b. Member meets any of the following criteria:
         i. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
         ii. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine or acitretin (see Appendix A).
         iii. Member has severe psoriasis that warrants a biologic DMARD as first-line therapy.

B. Active psoriatic arthritis (PsA)
   Authorization of 24 months may be granted for treatment of active psoriatic arthritis in members who are 18 years of age or older.

C. Moderately to severely active Crohn’s disease (CD)
   1. Authorization of 24 months may be granted for members who are 18 years of age or older who have previously received Stelara or any other biologic indicated for the treatment of Crohn’s disease.
2. Authorization of 24 months may be granted for treatment of moderately to severely active CD in members who are 18 years of age or older who have had an inadequate response, intolerance or contraindication to EITHER of the following:
   a. At least ONE conventional therapy option (see Appendix B)
   b. At least ONE TNF-alpha inhibitor indicated for CD:
      i. Cimzia (certolizumab)
      ii. Humira (adalimumab)
      iii. Remicade (infliximab)

III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 4 months of therapy with Stelara as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB).

Note: Members who have received Stelara or any other biologic DMARD or targeted synthetic DMARD (e.g. Xeljanz) are exempt from requirements related to TB screening in this Policy.

Stelara for intravenous administration is FDA-approved for the treatment of Crohn’s disease and will only be authorized for this condition.

V. APPENDICES

Appendix A: Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin.
1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Drug interaction
4. Cannot be used due to risk of treatment-related toxicity
5. Pregnancy or planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

Appendix B: Examples of Conventional Therapy Options for CD
1. Mild to moderate disease – induction of remission:
   a. Oral budesonide
   b. Alternatives: metronidazole, ciprofloxacin, rifaximin
2. Mild to moderate disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternatives: oral budesonide, methotrexate intramuscular (IM) or subcutaneous (SC), sulfasalazine
3. Moderate to severe disease – induction of remission:
   a. Prednisone, methylprednisolone intravenously (IV)
   b. Alternatives: methotrexate IM or SC
4. Moderate to severe disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: methotrexate IM or SC
5. Perianal and fistulizing disease – induction of remission:
   a. Metronidazole ± ciprofloxacin, tacrolimus
6. Perianal and fistulizing disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: methotrexate IM or SC

VI. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

STIMATE (desmopressin acetate nasal spray)

POLICY*

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Hemophilia A with factor VIII level >5%
   2. Mild to moderate type 1 von Willebrand disease (vWD) with Factor VIII level >5%

B. Compendial Uses
   1. Type 2A, 2M, 2N vWD
   2. Qualitative platelet disorders
   3. Acquired hemophilia A
   4. Acquired von Willebrand syndrome

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Von Willebrand Disease
   1. Type 1 vWD
      Indefinite authorization may be granted for treatment of mild or moderate type 1 vWD.
   2. Type 2A, 2M, or 2N vWD
      a. Authorization of one month may be granted for treatment of type 2A, 2M, or 2N vWD in members who are initiating therapy.
      b. Indefinite authorization may be granted for treatment of type 2A, 2M, or 2N vWD in members who are continuing therapy and have demonstrated a response to an initial trial of Stimate.

B. Hemophilia A
   Indefinite authorization may be granted for treatment of hemophilia A with factor VIII activity level greater than 5% (see Appendix).

C. Qualitative Platelet Disorders
   Indefinite authorization may be granted for treatment of a qualitative platelet disorder.

D. Acquired Hemophilia A
   Indefinite authorization may be granted for treatment of acquired hemophilia A.

E. Acquired von Willebrand Syndrome
Indefinite authorization may be granted for treatment of acquired von Willebrand syndrome.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. APPENDIX

Appendix: Classification of Hemophilia by Clotting Factor Level (% Activity) and Bleeding Episodes

<table>
<thead>
<tr>
<th>Severity</th>
<th>Clotting Factor Level % activity*</th>
<th>Bleeding Episodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe</td>
<td>&lt;1%</td>
<td>Spontaneous bleeding episodes, predominantly into joints and muscles</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Severe bleeding with trauma, injury or surgery</td>
</tr>
<tr>
<td>Moderate</td>
<td>1% to 5%</td>
<td>Occasional spontaneous bleeding episodes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Severe bleeding with trauma, injury or surgery</td>
</tr>
<tr>
<td>Mild</td>
<td>6% to 40%</td>
<td>Severe bleeding with serious injury, trauma or surgery</td>
</tr>
</tbody>
</table>

*Factor assay levels are required to determine the diagnosis and are of value in monitoring treatment response.12

*Note: This program addresses the appropriate use of Stimate Nasal Spray only. Stimate Nasal Spray and DDAVP (desmopressin) Nasal Spray are two distinct products and are not interchangeable. DDAVP Nasal Spray is not indicated for hemophilia or VWD.

V. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

STIVARGA (regorafenib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Stivarga is indicated for the treatment of patients with metastatic colorectal cancer (CRC) who have been previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-vascular endothelial growth factor (VEGF) therapy, and, if RAS wild type, an anti-epidermal growth factor receptor (EGFR) therapy.
   2. Stivarga is indicated for the treatment of patients with locally advanced, unresectable or metastatic gastrointestinal stromal tumor (GIST) who have been previously treated with imatinib mesylate and sunitinib malate.
   3. Stivarga is indicated for the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

B. Compendial Uses
   1. Unresectable, advanced, or metastatic colorectal cancer that was not previously treated with Stivarga
   2. Progressive Gastrointestinal Stromal Tumors (GIST)

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Colorectal Cancer (CRC)
   Authorization of 12 months may be granted for the treatment of unresectable, advanced, or metastatic colorectal cancer when the member has progressed on treatment with either of the following:
   1. FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, and irinotecan) regimen, OR
   2. Irinotecan- AND oxaliplatin-based regimens

B. Gastrointestinal stromal tumor (GIST)
   Authorization of 12 months may be granted for the treatment of progressive disease in members who have been previously treated with imatinib or sunitinib.

C. Hepatocellular carcinoma
   Authorization of 12 months may be granted for the treatment of hepatocellular carcinoma in members who have been previously treated with sorafenib.

III. CONTINUATION OF THERAPY

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All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

STRENSIQ (asfotase alfa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Strensiq is indicated for the treatment of patients with perinatal/infantile- and juvenile-onset hypophosphatasia (HPP).

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review:

Submission of the following:
A. Documentation of presence of condition before the age of 18, if applicable
B. Documentation confirming diagnosis which include one of the following:
   1. Genetic testing results confirming a mutation in the ALPL gene
   2. Submission of ALL of the following:
      i. Radiographic imaging demonstrating skeletal abnormalities (See Appendix)
      ii. A serum alkaline phosphatase level below the gender and age-specific reference range of the laboratory performing the test
      iii. Elevated TNSALP substrate level (i.e., serum PLP level, serum or urine PEA level, urinary PPi level)

III. CRITERIA FOR INITIAL APPROVAL

Perinatal/infantile- and juvenile-onset hypophosphatasia (HPP) 1-4

Authorization of 12 months may be granted for treatment of HPP when all of the following criteria are met:

A. The member has clinical signs and/or symptoms of hypophosphatasia (See Appendix A)
B. The onset of the disease was perinatal/infantile or juvenile. If the member is 18 years of age or older at the time of the request, documentation of the presence of the condition before the age of 18 must be provided (e.g., member began experiencing symptoms at age 10).
C. The diagnosis was confirmed by one of the following (1 or 2):
   1. The presence of a known pathological mutation in the ALPL gene as detected by ALPL molecular genetic testing
   2. The diagnosis is supported by ALL of the following:
      i. Radiographic imaging demonstrating skeletal abnormalities (See Appendix B)
      ii. A serum alkaline phosphatase level below the gender- and age-specific reference range of the laboratory performing the test
iii. Elevated tissue-nonspecific alkaline phosphatase (TNSALP) substrate level (i.e., serum PLP level, serum or urine PEA level, urinary PPi level)

IV. CONTINUATION OF THERAPY

Authorization of 12 months will be granted for continued treatment in members requesting reauthorization for an indication listed in Section III are currently receiving the requested medication through a paid pharmacy or medical benefit and are experiencing benefit from therapy (e.g., improvement in skeletal manifestations, growth, gait/mobility, muscle strength).

V. APPENDIX

Appendix A. Examples of Signs and Symptoms of HPP²⁻⁴
A. Perinatal/infantile-onset HPP:
   - Generalized hypominerlization with rachitic features, chest deformities and rib fractures
   - Skeletal abnormalities (e.g., short limbs, abnormally shaped chest, soft skull bone)
   - Respiratory problems (e.g., pneumonia)
   - Hypercalcemia
   - Failure to thrive
   - Severe muscular hypotonia and weakness
   - Nephrocalcinosis secondary to hypercalciuria
   - Swallowing problems
   - Seizures

B. Juvenile-onset HPP:
   - Premature loss of deciduous teeth
   - Failure to thrive with anorexia, nausea, and gastrointestinal problems
   - Short stature with bowed legs or knock knees
   - Skeletal deformities (e.g., enlarged wrist and ankle joints, abnormal skull shape)
   - Bone and joint pain
   - Rickets
   - Fractures
   - Delayed walking
   - Waddling gait

Appendix B. Examples of Radiographic Findings that Support HPP Diagnosis ²⁻⁴
- Infantile rickets
- Alveolar bone loss
- Focal bony defects of the metaphyses
- Metatarsal stress fractures
- Osteomalacia with lateral pseudofractures
- Osteopenia, osteoporosis, or low bone mineral content for age (as detected by dual-energy x-ray absorptiometry [DEXA])

VI. REFERENCES


PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>NARCOLEPSY AGENTS</th>
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<tbody>
<tr>
<td>BRAND NAME*</td>
<td>(generic)</td>
</tr>
<tr>
<td></td>
<td>SUNOSI</td>
</tr>
<tr>
<td></td>
<td>(solriamfetol)</td>
</tr>
</tbody>
</table>

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Quantity Limit

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS
Sunosi is indicated to improve wakefulness in adult patients with excessive daytime sleepiness associated with narcolepsy or obstructive sleep apnea (OSA).

Limitations of use
Sunosi is not indicated to treat the underlying airway obstruction in OSA. Ensure that the underlying airway obstruction is treated (e.g., with continuous positive airway pressure (CPAP)) for at least one month prior to initiating Sunosi for excessive daytime sleepiness. Modalities to treat the underlying airway obstruction should be continued during treatment with Sunosi. Sunosi is not a substitute for these modalities.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has narcolepsy confirmed by sleep lab evaluation
  AND
  o The patient has experienced an inadequate treatment response, intolerance or contraindication to a CNS stimulant (e.g., amphetamine, dextroamphetamine, methylphenidate)
  AND
  o The patient has experienced an inadequate treatment response, intolerance or contraindication to modafinil OR armodafinil

OR
- The patient has obstructive sleep apnea (OSA) confirmed by polysomnography
  AND
  o The patient has been receiving treatment for the underlying airway obstruction (e.g., continuous positive airway pressure [CPAP]) for at least one month
  AND
  o The patient has experienced an inadequate treatment response, intolerance or contraindication to modafinil OR armodafinil

Quantity Limits Apply.

RATIONALE
The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Sunosi is indicated to improve wakefulness in adult patients with excessive daytime sleepiness associated with narcolepsy or obstructive sleep apnea (OSA). Sunosi is not indicated to treat the underlying airway obstruction in OSA. Ensure that the underlying airway obstruction is treated (e.g., with continuous positive airway pressure (CPAP)) for at least one month prior to initiating Sunosi for excessive...
daytime sleepiness. Modalities to treat the underlying airway obstruction should be continued during treatment with Sunosi. Sunosi is not a substitute for these modalities.

According to the American Academy of Sleep Medicine (AASM), successful treatment of hypersomnia of central origin requires an accurate diagnosis, individual tailoring of therapy to produce the fullest possible return of normal function, and regular follow-up to monitor response to treatment. The evaluation should include a thorough evaluation of other possible contributing causes of excessive daytime sleepiness. The International Classification of Sleep Disorders, Third Edition (ICSD-3) specifies necessary diagnostic tests and criteria for each disorder of central origin. For narcolepsy, a sleep lab evaluation consisting of an overnight polysomnography (PSG) and mean sleep latency tests (MSLT) is recommended to confirm the diagnosis. Many other conditions produce such sleepiness and can mimic or coexist with a hypersomnia of central origin.4

According to AASM guidelines, modafinil is effective for treatment of daytime sleepiness due to narcolepsy. One additional study of 196 subjects involved assessment of armodafinil (the longer half-life enantiomer of modafinil) for treatment of excessive sleepiness in patients with narcolepsy.4 Subjects receiving armodafinil experienced significant improvement in sleepiness as measured by the Mean Wakefulness Test (MWT) mean sleep latency, and in the Clinical Global Impression of Change.4 The guidelines also state that amphetamine, dextroamphetamine, and methylphenidate are effective for treatment of daytime sleepiness due to narcolepsy.4 Therefore, patients with narcolepsy who have an inadequate treatment response, intolerance, or contraindication to a CNS stimulant and either modafinil or armodafinil will be considered for approval.

The presence or absence of obstructive sleep apnea (OSA) must be determined before initiating treatment. Diagnostic criteria for OSA are based on clinical signs and symptoms determined during a comprehensive sleep evaluation, which includes a sleep oriented history and physical examination, and findings defined by sleep testing.5 Following the history and physical examination, patients can be stratified according to their OSA disease risk. Those patients deemed high risk should have the diagnosis confirmed and severity determined with objective testing such as polysomnography with respiratory monitoring.5 OSA should be approached as a chronic disease requiring long-term, multidisciplinary management. The patient should be an active participant in the decision on treatment type and taught to contribute to the management of his or her own disease. Positive airway pressure (PAP) is the treatment of choice for mild, moderate, and severe OSA and should be offered as an option to all patients. Alternative therapies may be offered depending on the severity of the OSA and the patient’s anatomy, risk factors, and preferences.5 Oral appliances (OA) may improve upper airway patency during sleep by enlarging the upper airway and/or by decreasing upper airway collapsibility (e.g., improving upper airway muscle tone). Although not as efficacious as PAP, OAs are indicated for use in patients with mild to moderate OSA who prefer OAs to CPAP or who do not respond to CPAP, are not appropriate candidates for CPAP, or who fail CPAP or other measures.5 Patients should be established on effective treatment of the underlying airway obstruction associated with OSA before considering pharmacologic therapy for excessive sleepiness associated with OSA.5 Patients should be continued on their treatment for the underlying airway obstruction while using pharmacologic treatment for excessive sleepiness due to OSA.1-3,5 Therefore, patients with OSA must be established on therapy to treat the underlying obstruction for approval of Sunosi.

Modafinil is recommended for the treatment of residual excessive daytime sleepiness in OSA patients who have sleepiness despite effective positive airway pressure (PAP) treatment and who are lacking any other identifiable cause for their sleepiness. Before using modafinil, other causes of residual sleepiness must be ruled out including: suboptimal objective adherence with PAP; ill-fitting PAP masks; insufficient sleep; poor sleep hygiene; other sleep disorders such as narcolepsy or restless legs syndrome/periodic limb movements of sleep; and depression. Modafinil should be used in addition to PAP therapy.5 Armodafinil (the longer half-life enantiomer of modafinil) is also indicated for the treatment of excessive daytime sleepiness associated with obstructive sleep apnea.2,3 Patients with OSA who have an inadequate treatment response, intolerance, or contraindication to modafinil or armodafinil will be considered for approval.

The recommended starting dosage of Sunosi in patients with narcolepsy is 75 mg once daily. Based on efficacy and tolerability, the dosage may be doubled at intervals of at least 3 days to a maximum recommended dose of 150 mg once daily. For OSA, Sunosi should be initiated at 37.5 mg once daily and may be doubled based on efficacy and tolerability at intervals of at least 3 days to a maximum recommended dose of 150 mg daily. Doses above 150 mg daily do not confer increased effectiveness sufficient to outweigh dose-related adverse reactions. Sunosi is available as 75 mg tablets that...
are scored and can be split in half, and as 150 mg tablets. Therefore, the approval will be limited to a maximum of 30 tablets per month.

REFERENCES

CRITERIA FOR APPROVAL

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Does the patient have a diagnosis of narcolepsy confirmed by sleep lab evaluation?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>[If no, then skip to question 3.]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Has the patient experienced an inadequate treatment response, intolerance, or contraindication to a central nervous system (CNS) stimulant (e.g., amphetamine, dextroamphetamine, methylphenidate)?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>[If yes, then skip to question 5.]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Does the patient have a diagnosis of obstructive sleep apnea (OSA) confirmed by polysomnography?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>4. Has the patient been receiving treatment for the underlying airway obstruction (e.g., continuous positive airway pressure [CPAP]) for at least one month?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>5. Has the patient experienced an inadequate treatment response, intolerance, or contraindication to armodafinil OR modafinil?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>6. Does the patient require MORE than the plan allowance of 30 tablets per month?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>[RPh Note: If yes, then deny and enter a partial approval for 30 tablets per month.]</td>
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Mapping Instructions

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
<th>DENIAL REASONS – DO NOT USE FOR MEDICARE PART D</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Go to 2</td>
<td>Go to 3</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have tried a central nervous system (CNS) stimulant drug (e.g., amphetamine, dextroamphetamine, or methylphenidate) and it either did not work for you, or you cannot use it. Your request has been denied based on the information we have.</td>
</tr>
<tr>
<td>2. Go to 5</td>
<td>Deny</td>
<td></td>
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</tbody>
</table>

CRITERIA FOR APPROVAL

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Does the patient have a diagnosis of narcolepsy confirmed by sleep lab evaluation?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>[If no, then skip to question 3.]</td>
<td></td>
<td></td>
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<tr>
<td>2. Has the patient experienced an inadequate treatment response, intolerance, or contraindication to a central nervous system (CNS) stimulant (e.g., amphetamine, dextroamphetamine, methylphenidate)?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>[If yes, then skip to question 5.]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Does the patient have a diagnosis of obstructive sleep apnea (OSA) confirmed by polysomnography?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>4. Has the patient been receiving treatment for the underlying airway obstruction (e.g., continuous positive airway pressure [CPAP]) for at least one month?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>5. Has the patient experienced an inadequate treatment response, intolerance, or contraindication to armodafinil OR modafinil?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>6. Does the patient require MORE than the plan allowance of 30 tablets per month?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>[RPh Note: If yes, then deny and enter a partial approval for 30 tablets per month.]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>[Short Description: No inadequate response, intolerance, or contraindication to a CNS stimulant drug]</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
</tbody>
</table>
| 3. | Go to 4 | Deny | You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions:
- You have narcolepsy confirmed by sleep lab testing
- You have obstructive sleep apnea confirmed by testing
Your request has been denied based on the information we have. [Short Description: No approvable diagnosis] |
| 4. | Go to 5 | Deny | You do not meet the requirements of your plan. Your plan covers this drug when you have been on treatment for airway problems due to obstructive sleep apnea for at least one month. Your request has been denied based on the information we have. [Short Description: No underlying treatment for OSA] |
| 5. | Go to 6 | Deny | You do not meet the requirements of your plan. Your plan covers this drug when you have tried armodafinil or modafinil and it did not work for you, or you cannot use it. Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance, or contraindication to armodafinil or modafinil] |
| 6. | Deny | Approve, 12 months, 30 tablets/25 days* or 90 tablets/75 days* | You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 30 tablets/month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity] |

*The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.
SPECIALTY GUIDELINE MANAGEMENT

Supprelin LA (histrelin acetate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
   Supprelin LA is indicated for the treatment of children with central precocious puberty (CPP).

B. Compendial Use
   Gender Dysphoria (also known as gender non-conforming or transgender persons)
   NOTE: Some plans may opt-out of coverage for gender dysphoria.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Central precocious puberty (CPP)
   1. Authorization up to age 12 may be granted for the treatment of CPP in a female member when all of the following criteria are met:
      a. The diagnosis of CPP has been confirmed by a pubertal response to a gonadotropin releasing hormone (GnRH) agonist test or a pubertal level of a third generation luteinizing hormone (LH) assay.
      b. The assessment of bone age versus chronological age supports the diagnosis of CPP.
      c. The member was less than 8 years of age at the onset of secondary sexual characteristics.
   2. Authorization up to age 13 may be granted for the treatment of CPP in a male member when all of the following criteria are met:
      a. The diagnosis of CPP has been confirmed by a pubertal response to a GnRH agonist test or a pubertal level of a third generation LH assay.
      b. The assessment of bone age versus chronological age supports the diagnosis of CPP.
      c. The member was less than 9 years of age at the onset of secondary sexual characteristics.

B. Gender dysphoria
   1. Authorization of 12 months may be granted for pubertal suppression in preparation for gender reassignment in an adolescent member when all of the following criteria are met:
      a. The member has a diagnosis of gender dysphoria.
      b. The member has reached Tanner stage 2 of puberty.
   2. Authorization of 12 months may be granted for gender reassignment in an adult member when all of the following criteria are met:
      a. The member has a diagnosis of gender dysphoria.
      b. The member will receive Supprelin LA concomitantly with cross sex hormones.
III. CONTINUATION OF THERAPY

A. Central precocious puberty (CPP)
   1. Authorization up to age 12 may be granted for continuation of therapy for CPP in a female member if the member is currently less than 12 years of age.
   2. Authorization up to age 13 may be granted for continuation of therapy for CPP in a male member if the member is currently less than 13 years of age.

B. Gender Dysphoria
   All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

SUTENT (sunitinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Gastrointestinal Stromal Tumor (GIST)
   Sutent is indicated for the treatment of gastrointestinal stromal tumor after disease progression on or intolerance to imatinib mesylate.

2. Advanced Renal Cell Carcinoma (RCC)
   Sutent is indicated for the treatment of advanced renal cell carcinoma.

3. Adjuvant Treatment of Renal Cell Carcinoma (RCC)
   Sutent is indicated for the adjuvant treatment of adult patients at high risk of recurrent RCC following nephrectomy.

4. Advanced Pancreatic Neuroendocrine Tumors (pNET)
   Sutent is indicated for the treatment of progressive, well-differentiated pancreatic neuroendocrine tumors in patients with unresectable locally advanced or metastatic disease.

B. Compendial Uses

1. Relapsed or stage IV RCC
2. Soft tissue sarcoma subtypes:
   a. Angiosarcoma; as single-agent therapy
   b. Solitary fibrous tumor; as single-agent therapy
   c. Hemangiopericytoma, as single-agent therapy
   d. Alveolar soft part sarcoma; as single-agent therapy
3. Gastrointestinal stromal tumors
   a. Primary treatment for patients with life-threatening side effects on imatinib therapy and with disease documented as resectable with negative margins but with risk of significant morbidity, unresectable, recurrent, or metastatic
   b. Postoperative treatment for patients who have life-threatening side effects on imatinib therapy
   c. Treatment for limited or generalized progressive disease following progression on imatinib
   d. Treatment in combination with everolimus for disease progression after single-agent therapy with imatinib, sunitinib, and regorafenib
4. Thymomas and thymic carcinomas, second-line therapy as a single agent
5. Thyroid carcinoma (papillary, Hürthle cell, or follicular), progressive and/or symptomatic iodine-refractory
6. Medullary thyroid carcinoma
   a. Clinical trials, vandetanib, or cabozantinib are not available or appropriate
   b. Disease progression on vandetanib or cabozantinib
7. Meningioma; surgically inaccessible recurrent or progressive disease for which radiation is not possible
8. Recurrent chordoma; as single-agent therapy
All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Renal Cell Carcinoma
   1. Authorization of 12 months may be granted for treatment of relapsed or metastatic renal cell carcinoma when any of the following criteria are met:
      a. Sutent is given as first-line or subsequent therapy for disease with clear cell histology; OR
      b. Sutent is given as systemic therapy for disease with non-clear cell histology.
   2. Authorization of up to 54 weeks total may be granted for adjuvant treatment of members who are at high risk of recurrent renal cell carcinoma following nephrectomy.

B. Soft Tissue Sarcoma
   Authorization of 12 months may be granted for treatment of the following subtypes of soft tissue sarcoma as single-agent therapy: alveolar soft-part sarcoma, angiosarcoma, solitary fibrous tumor, or hemangiopericytoma.

C. Gastrointestinal Stromal Tumor (GIST)
   1. Authorization of 12 months may be granted for treatment of gastrointestinal stromal tumor after failure of imatinib due to progression or intolerable side effects.
   2. Authorization of 12 months may be granted for treatment of gastrointestinal stromal tumor in combination with everolimus for disease progression after single-agent therapy with imatinib, sunitinib, and regorafenib.

D. Pancreatic Neuroendocrine Tumor
   Authorization of 12 months may be granted for treatment of unresectable locally advanced or metastatic pancreatic neuroendocrine tumors.

E. Thymoma and Thymic Carcinoma
   Authorization of 12 months may be granted for treatment of thymoma or thymic carcinoma with failure of one previous chemotherapy regimen.

F. Thyroid Carcinoma
   Authorization of 12 months may be granted for treatment of progressive and/or symptomatic radioiodine refractory papillary, Hurthle cell, or follicular thyroid carcinoma.

G. Medullary Thyroid Carcinoma
   Authorization of 12 months may be granted for treatment of metastatic medullary thyroid carcinoma when either of the following criteria are met:
   1. Member has a contraindication or intolerance to vandetanib (Caprelsa) AND cabozantinib (Cometriq); OR
   2. Disease progression occurred while on vandetanib (Caprelsa) OR cabozantinib (Cometriq)

H. Meningioma
   Authorization of 12 months may be granted for treatment of surgically inaccessible recurrent or progressive meningioma for which radiation is not possible.
I. Chordoma
Authorization of 12 months may be granted for treatment of recurrent chordoma as single-agent therapy.

III. CONTINUATION OF THERAPY
A. Authorization of 12 months may be granted for continued treatment in members requesting reauthorization who have not experienced disease progression or an unacceptable toxicity for the specified indications below:
1. Relapsed or metastatic renal cell carcinoma
2. Soft tissue sarcoma
3. Gastrointestinal stromal tumor
4. Pancreatic neuroendocrine tumor
5. Thymoma and thymic carcinoma
6. Thyroid carcinoma
7. Medullary thyroid carcinoma
8. Meningioma
9. Chordoma

B. Authorization of up to 54 weeks total may be granted for continued treatment in members requesting reauthorization for adjuvant treatment of renal cell carcinoma when the following criteria are met:
1. Disease is not recurrent; AND
2. Member has not exceeded a maximum of nine 6 week cycles.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

SYLATRON (peginterferon alfa-2b)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
   1. SYLATRON is indicated for the adjuvant treatment of melanoma with microscopic or gross nodal involvement within 84 days of definitive surgical resection including complete lymphadenectomy.

B. Compendial Uses
   1. Low-risk myelofibrosis
   2. Polycythemia vera
   3. Essential thrombocythemia
   4. Systemic mastocytosis

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Melanoma
   Authorization of 12 months may be granted for the treatment of melanoma.

B. Myelofibrosis
   Authorization of 12 months may be granted for the treatment of myelofibrosis.

C. Polycythemia Vera
   Authorization of 12 months may be granted for the treatment of polycythemia vera.

D. Essential Thrombocythemia
   Authorization of 12 months may be granted for the treatment of essential thrombocythemia.

E. Systemic Mastocytosis
   Authorization of 12 months may be granted for the treatment of systemic mastocytosis.

III. CONTINUATION OF THERAPY

A. Systemic mastocytosis
Authorization of 12 months may be granted if the patient is experiencing benefit from therapy as evidenced by improvement in symptoms and/or disease markers (e.g., reduction in serum and urine metabolites of mast cell activation, improvement in cutaneous lesions, skeletal disease, bone marrow mast cell burden, etc.)

B. All Other Indications
Authorization of 12 months may be granted for continuation of therapy for an indication outlined in section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

SYLVANT (siltuximab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Sylvant is indicated for the treatment of patients with multicentric Castleman’s disease who are human immunodeficiency virus (HIV) negative and human herpesvirus-8 (HHV-8) negative.

B. Compendial Use

Relapsed/refractory unicentric Castleman’s disease

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Multicentric Castleman’s disease or relapsed/refractory unicentric Castleman’s disease. Authorization of 12 months may be granted for the treatment of multicentric Castleman’s disease or relapsed/refractory unicentric Castleman’s disease.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

SYMDEKO (tezacaftor/ivacaftor)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Symdeko is indicated for the treatment of patients with cystic fibrosis (CF) aged 6 years and older who are homozygous for the F508del mutation or who have at least one mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene that is responsive to tezacaftor/ivacaftor based on in vitro data and/or clinical evidence. If the patient’s genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of CFTR mutation followed by verification with bi-directional sequencing when recommended by the mutation test instructions for use.

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review: genetic testing report confirming the presence of the appropriate CFTR gene mutation.

III. CRITERIA FOR INITIAL APPROVAL

Cystic Fibrosis
Indefinite authorization may be granted for treatment of cystic fibrosis when all of the following criteria are met:
A. Genetic testing was conducted to detect a mutation in the CFTR gene.
C. The member is at least 6 years of age.
D. Symdeko will not be used in combination with Kalydeco or Orkambi.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

SYNAGIS (palivizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Synagis is indicated for the prevention of serious lower respiratory tract disease caused by respiratory syncytial virus (RSV) in pediatric patients:
- with a history of premature birth (less than or equal to 35 weeks gestational age) and who are 6 months of age or younger at the beginning of RSV season,
- with bronchopulmonary dysplasia (BPD) that required medical treatment within the previous 6 months and who are 24 months of age or younger at the beginning of RSV season,
- with hemodynamically significant congenital heart disease (CHD) and who are 24 months of age or younger at the beginning of RSV season

Limitations of Use:
The safety and efficacy of Synagis have not been established for treatment of RSV disease.

B. Compendial Uses

1. RSV prophylaxis in infants with congenital abnormalities of the airway or neuromuscular disease that compromise handling of respiratory secretions
2. RSV prophylaxis in immunocompromised pediatric patients
3. RSV prophylaxis in pediatric patients with cystic fibrosis who have evidence of chronic lung disease or nutritional compromise in the first year of life

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of up to 5 doses per RSV season may be granted for the prevention of serious lower respiratory tract disease caused by RSV when a member has any of the following diagnoses and meets the criteria pertaining to the diagnosis:
1. Prematurity
2. Chronic lung disease (CLD) of prematurity
3. Congenital heart disease (CHD) (See Appendix B)
4. Congenital airway abnormality
5. Neuromuscular condition
6. Immunocompromised children
7. Cystic fibrosis

A. Prematurity
All of the following criteria are met:
1. Member’s gestational age is < 29 weeks, 0 days.
2. Member’s chronological age at the start of RSV season is < 12 months.

B. CLD of prematurity
ALL of the following criteria must be met:
1. Member’s gestational age is < 32 weeks, 0 days.
2. Requirement for > 21% oxygen for at least the first 28 days after birth.
3. Member meets either of the following criteria:
   i. Member’s chronological age at the start of their first RSV season is < 12 months.
   ii. Member’s chronological age at the start of the subsequent RSV season is < 24 months and the member continues to require medical support (e.g., chronic corticosteroids, diuretic therapy, supplemental oxygen) during the 6-month period prior to the start of the RSV season.

C. CHD
All of the following criteria are met:
1. CHD is hemodynamically significant.
2. Member meets either of the following criteria:
   i. Member’s chronological age at the start of RSV season is < 12 months.
   ii. Member’s chronological age at the start of the subsequent RSV season is between 12 to 24 months and the member will be undergoing cardiac transplantation during the RSV season.

D. Congenital airway abnormality
All of the following criteria must be met:
1. The condition compromises handling of respiratory secretions.
2. Member’s chronological age at the start of RSV season is < 12 months.

E. Neuromuscular condition
All of the following criteria must be met:
1. The condition compromises handling of respiratory secretions.
2. Member’s chronological age at the start of RSV season is < 12 months.

F. Immunocompromised children
All of the following criteria must be met:
1. Member is profoundly immunocompromised during the RSV season (e.g., SCID, stem cell transplant, bone marrow transplant)
2. Member’s chronological age at the start of the RSV season is <24 months

G. Cystic Fibrosis
Either of the following criteria must be met:
1. Member’s chronological age at the start of the RSV season is < 12 months and the member has evidence of CLD or nutritional compromise
2. Member’s chronological age at the start of RSV season is between 12 to 24 months and the member has manifestations of lung disease (e.g., hospitalizations for pulmonary exacerbations) or weight less than the 10th percentile

III. OTHER

For all off-season Synagis requests, authorization of 1 dose per request, up to a maximum of 5 doses per RSV season, may be granted if the RSV activity for the requested region is ≥ 10% within 2 weeks of the intended dose according to the CDC National Respiratory and Enteric Virus Surveillance System (NREVSS). The local
health department or the CDC NREVSS will be consulted to assess the RSV activity for that region (http://www.cdc.gov/surveillance/nrevss/rsv/index.html). Other Specialty Guideline Management criteria apply.

CVS Caremark PBM Synagis Season for 2019-2020 will be November 1, 2019 to March 31, 2020. Other health plans may differ.

IV. APPENDIX

**Appendix A: Recommended Use of Synagis for Prevention of RSV Infection**

Recommendations from the American Academy of Pediatrics for the prevention of RSV infection with Synagis are summarized in Table below. Synagis should be administered intramuscularly at a dose of 15 mg/kg once per month beginning prior to the onset of the RSV season, which typically occurs in November. Because 5 monthly doses of Synagis will provide more than 6 months of serum Synagis concentrations above the desired serum concentration for most infants, administration of more than 5 monthly doses is not recommended within the continental United States.

**Table. Recommended Use of Synagis for Prevention of RSV Infection**

| Prematurity | • Preterm infants born < 29 weeks, 0 days of gestation who are younger than 12 months at the start of the RSV season |
| Congenital Heart Disease | • Infants and children < 12 months of age with hemodynamically significant CHD  
  • Those most likely to benefit from prophylaxis include:  
    o Infants with acyanotic heart disease who are receiving medication to control congestive heart failure and will require cardiac surgical procedures  
    o Infants with moderate to severe pulmonary hypertension  
  • Infants and children < 24 months of age who undergo cardiac transplantation during the RSV season |
| Chronic Lung Disease of Prematurity | • For the first RSV season during the first year of life: Preterm infants who develop CLD of prematurity defined as:  
  o Gestational age < 32 weeks, 0 days AND  
  o Requirement for > 21% oxygen for at least the first 28 days after birth  
  • For the second RSV season during the second year of life: Preterm infants who:  
    o Satisfy the above definition of CLD of prematurity AND  
    o Continue to require medical support* for CLD during the 6-month period prior to the start of the second RSV season |
| Congenital Abnormality of the Airway/ Neuromuscular Condition | • Infants who have either a significant congenital abnormality of the airway or a neuromuscular condition that compromises handling of respiratory secretions for the first year of life |
**Immunocompromised children**
- Children younger than 24 months of age who are profoundly immunocompromised during the RSV season

**Cystic Fibrosis**
- For the first year of life, children with clinical evidence of CLD and/or nutritional compromise
- For the second year of life, children with manifestations of severe lung disease (previous hospitalization for pulmonary exacerbation in the first year of life or abnormalities on chest radiography or chest computed tomography that persist when stable) OR weight for length less than the 10th percentile.

Abbreviations: CHD = congenital heart disease; CLD = chronic lung disease (formerly bronchopulmonary dysplasia); RSV = respiratory syncytial virus.

* Medical support includes supplemental oxygen, diuretic therapy, or chronic corticosteroid therapy.

**Appendix B: Examples of Congenital Heart Anomalies**
- Atrial or ventricular septal defect
- Coarctation of aorta
- Tetralogy of Fallot
- Pulmonary or aortic valve stenosis
- Tricuspid atresia
- Ebstein’s anomaly
- Pulmonary atresia
- Transposition of great arteries
- Truncus arteriosus
- Hypoplastic left/right ventricle
- Single ventricle
- Double-outlet right ventricle
- Total anomalous pulmonary venous return

*Must be hemodynamically significant. See Table above for examples of infants and children who are most likely to benefit from Synagis.

**V. REFERENCES**

Synagis 1988-A SGM P2019

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SPECIALTY GUIDELINE MANAGEMENT

SYNRIBO (omacetaxine mepesuccinate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
   Adult patients with chronic or accelerated phase chronic myeloid leukemia (CML) with resistance and/or intolerance to two or more tyrosine kinase inhibitors (TKIs)

B. Compendial Use
   1. Primary treatment of advanced phase CML for patients with disease progression to accelerated phase
   2. Follow-up therapy for CML patients after hematopoietic stem cell transplant (HSCT)
   3. Patients with a T315I mutation or disease that is resistant and/or intolerant to two or more tyrosine kinase inhibitors (TKIs)

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review:

A. Prior to initiation of therapy: results of cytogenetic and/or molecular testing for detection of the Ph chromosome or the BCR-ABL gene

B. For members requesting initiation of Synribo therapy for treatment of T315I-positive CML: results of T315I mutation testing

III. CRITERIA FOR INITIAL APPROVAL

Chronic Myeloid Leukemia (CML)
Authorization of 6 months may be granted for treatment of chronic or accelerated phase CML confirmed by detection of the BCR-ABL gene by cytogenetic and/or molecular testing when any of the following criteria are met:

A. Member has a T315I mutation
B. Member has experienced resistance, toxicity, or intolerance to prior therapy with two or more TKIs (e.g., imatinib, bosutinib, dasatinib, nilotinib, ponatinib)
C. Disease has progressed to accelerated phase
D. Member has received HSCT for CML
IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment of CML that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when either of the following criteria are met:

A. Member has not experienced disease progression or an unacceptable toxicity
B. Member has received HSCT

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

Adcirca (tadalafil)
tadalafil tablets (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) to improve exercise ability. Studies establishing effectiveness included predominately patients with NYHA Functional Class II – III symptoms and etiologies of idiopathic or heritable PAH (61%) or PAH associated with connective tissue diseases (23%).

B. Compendial Use

Secondary Raynaud’s phenomenon

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Pulmonary Arterial Hypertension

Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:
1. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
2. PAH was confirmed by either criterion (1) or criterion (2) below:
   i. Pretreatment right heart catheterization with all of the following results:
      a. mPAP ≥ 25 mmHg
      b. PCWP ≤ 15 mmHg
      c. PVR > 3 Wood units
   ii. For infants less than one year of age with any of the following conditions, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed:
      a. Post cardiac surgery
      b. Chronic heart disease
      c. Chronic lung disease associated with prematurity
      d. Congenital diaphragmatic hernia

B. Secondary Raynaud’s Phenomenon

Authorization of 12 months may be granted for treatment of secondary Raynaud’s phenomenon when the patient has had an inadequate response to one of the following medications:
1. Calcium channel blockers
2. Angiotensin receptor blockers
3. Selective serotonin reuptake inhibitors
4. Alpha blockers
III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section II who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. APPENDIX

WHO Classification of Pulmonary Hypertension
1 PAH
1.1 Idiopathic (PAH)
1.2 Heritable PAH
1.3 Drug- and toxin-induced PAH
1.4. PAH associated with:
   1.4.1 Connective tissue diseases
   1.4.2 HIV infection
   1.4.3 Portal hypertension
   1.4.4 Congenital heart diseases
   1.4.5 Schistosomiasis
1.5 PAH long-term responders to calcium channel blockers
1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease
2.1 PH due to heart failure with preserved LVEF
2.2 PH due to heart failure with reduced LVEF
2.3 Valvular heart disease
2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia
3.1 Obstructive lung disease
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction
4.1 Chronic thromboembolic PH
4.2 Other pulmonary artery obstructions
   4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
   4.2.2 Other malignant tumors
      Renal carcinoma
      Uterine carcinoma
      Germ cell tumours of the testis
      Other tumours
   4.2.3 Non-malignant tumours
      Uterine leiomyoma
   4.2.4 Arteritis without connective tissue disease
   4.2.5 Congenital pulmonary artery stenosis
   4.2.6 Parasites
Hydatidosis

5 PH with unclear and/or multifactorial mechanisms

5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders

5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis

5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis

5.4 Complex congenital heart disease

V. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

TAFINLAR (dabrafenib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Tafinlar is indicated as a single agent for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test.
   2. Tafinlar is indicated, in combination with trametinib, for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test.
   3. Tafinlar is indicated, in combination with trametinib, for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation as detected by an FDA-approved test.
   4. Tafinlar is indicated, in combination with trametinib, for the adjuvant treatment of patients with melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test, and involvement of lymph node(s), following complete resection.
   5. Tafinlar is indicated, in combination with trametinib, for the treatment of patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) with BRAF V600E mutation and no satisfactory locoregional treatment options.

B. Compendial Uses
   1. Melanoma, BRAF V600 activating mutation-positive
   2. Brain metastases from melanoma
   3. NSCLC, BRAF V600E
   4. Glioma, BRAF V600 activating mutation-positive
   5. Meningioma, BRAF V600 activating mutation-positive
   6. Astrocytoma, BRAF V600 activating mutation-positive
   7. Papillary, follicular, Hürthle cell thyroid carcinoma
   8. Colorectal cancer, BRAF V600E activating mutation-positive

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of BRAF mutation documentation is necessary to initiate prior authorization review.

III. CRITERIA FOR INITIAL APPROVAL

A. Melanoma
   1. Authorization of 12 months may be granted for treatment of unresectable or metastatic cutaneous melanoma with a BRAF V600 activating mutation as a single agent or in combination with trametinib (Mekinist).
2. Authorization of 12 months may be granted for treatment of brain metastases from melanoma with a BRAF V600 activating mutation in combination with trametinib (Mekinist).
3. Authorization of 12 months may be granted for adjuvant treatment of cutaneous melanoma with a BRAF V600 activating mutation in combination with trametinib (Mekinist).

B. Non-Small Cell Lung Cancer (NSCLC)
Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive NSCLC as a single agent or in combination with trametinib (Mekinist).

C. Anaplastic Thyroid Cancer (ATC)
Authorization of 12 months may be granted for treatment of metastatic BRAF V600E mutation-positive ATC in combination with trametinib (Mekinist).

D. Central Nervous System Cancer
Authorization of 12 months may be granted for treatment of BRAF V600 mutation-positive gliomas, meningiomas, or astrocytomas.

E. Thyroid carcinoma
Authorization of 12 months may be granted for treatment of progressive and/or symptomatic radiiodine-refractory BRAF-activating mutation positive follicular, Hurthle cell, or papillary thyroid carcinoma.

F. Colorectal Cancer
Authorization of 12 months may be granted for treatment of unresectable advanced or metastatic colorectal cancer when the following criteria are met:
1. Tafinlar is used in combination with trametinib (Mekinist) and either cetuximab or panitumumab
2. Tumor is positive for BRAF V600E mutation.
3. Will be used as subsequent therapy

IV. CONTINUATION OF THERAPY
Authorization of 12 months may be granted for continuation of therapy for an indication outlined in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen. For patients using Tafinlar for adjuvant treatment of cutaneous melanoma, only 12 months of therapy total will be approved.

V. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

TAGRISSO (osimertinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Tagrisso is indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test.
   2. Tagrisso is indicated for the treatment of patients with metastatic epidermal growth factor receptor (EGFR) T790M mutation-positive non-small cell lung cancer (NSCLC), as detected by an FDA-approved test, who have progressed on or after EGFR tyrosine kinase inhibitor (TKI) therapy.

B. Compendial Uses
   1. EGFR mutation-positive recurrent, advanced or metastatic NSCLC.
   2. Brain metastases from sensitizing EGFR mutation-positive NSCLC.
   3. Brain metastases from EGFR T790M mutation-positive NSCLC.

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: EGFR mutation testing results.

III. CRITERIA FOR INITIAL APPROVAL

Non-small cell lung cancer (NSCLC)

Authorization of 12 months may be granted for treatment of recurrent, advanced, or metastatic NSCLC (including brain metastases from NSCLC) in members with sensitizing EGFR mutation-positive disease.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced an unacceptable toxicity.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

TAKHZYRO (lanadelumab-flyo)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Prophylaxis to prevent attacks of hereditary angioedema (HAE) in patients 12 years of age and older

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. C4 levels and C1 inhibitor functional and antigenic protein levels
B. F12, angiopoietin-1 or plasminogen gene mutation testing, if applicable
C. Chart notes confirming family history of angioedema, if applicable

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for prevention of hereditary angioedema attacks when the requested medication will not be used in combination with Cinryze or Haegarda and either of the following criteria is met:

A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing:
   1. C1 inhibitor (C1-INH) antigenic level is below the lower limit of normal as defined by the laboratory performing the test or
   2. Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test).

B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
   1. Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing, or
   2. Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy when all of the following criteria are met:

A. Member meets the criteria for initial approval.
B. Member has experienced reduction in frequency, severity, and/or duration of attacks since starting treatment.
V. REFERENCES
ENHANCED SPECIALTY GUIDELINE MANAGEMENT

TAKHZYRO (lanadelumab-flyo)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Prophylaxis to prevent attacks of hereditary angioedema (HAE) in patients 12 years of age and older

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. C4 levels and C1 inhibitor functional and antigenic protein levels
B. F12, angiopoietin-1 or plasminogen gene mutation testing, if applicable
C. Chart notes confirming family history of angioedema, if applicable

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for prevention of hereditary angioedema attacks when the requested medication will not be used in combination with Cinryze or Haegarda and either of the following criteria is met:
A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing:
   1. C1 inhibitor (C1-INH) antigenic level is below the lower limit of normal as defined by the laboratory performing the test or
   2. Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test).
B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
   1. Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing, or
   2. Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy when all of the following criteria are met:
A. Member meets the criteria for initial approval.
B. Member has experienced reduction in frequency, severity, and/or duration of attacks since starting treatment.
V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

TALTZ (ixekizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
1. Moderate to severe plaque psoriasis
2. Active psoriatic arthritis

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderate to severe plaque psoriasis
   1. Authorization of 24 months may be granted for members who are 18 years of age or older who have previously received Taltz, Otezla, or any other biologic DMARD indicated for the treatment of moderate to severe plaque psoriasis.
   2. Authorization of 24 months may be granted for treatment of moderate to severe plaque psoriasis in members who are 18 years of age and older when all of the following criteria are met:
      a. At least 5% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
      b. Member meets any of the following criteria:
         i. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
         ii. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine or acitretin (see Appendix).
         iii. Member has severe psoriasis that warrants a biologic DMARD as first-line therapy.

B. Active psoriatic arthritis (PsA)
   Authorization of 24 months may be granted for treatment of active psoriatic arthritis in members who are 18 years of age or older.

III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Taltz as evidenced by low disease activity or improvement in signs and symptoms of the condition.
IV. OTHER

For all indications: Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB).

Note: Members who have received Taltz or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) are exempt from requirements related to TB screening in this Policy.

V. APPENDIX

Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin
1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Cannot be used due to risk of treatment-related toxicity
4. Drug interaction
5. Pregnancy or planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VI. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

TALZENNA (talazoparib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Talzenna is indicated for the treatment of adult patients with deleterious or suspected deleterious germline breast cancer susceptibility gene (BRCA)-mutated (gBRCAm) human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer. Select patients for therapy based on an FDA-approved companion diagnostic for Talzenna.

B. Compendial Uses

Single agent therapy for recurrent or stage IV (M1) human epidermal growth factor receptor 2 (HER2)-negative, BRCA 1/2-germline mutated breast cancer

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Breast cancer

Authorization of 12 months may be granted for the treatment of human epidermal growth factor receptor 2 (HER2)-negative locally advanced, recurrent or metastatic breast cancer in members with deleterious or suspected deleterious germline BRCA mutations as detected by an FDA-approved companion diagnostic test.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

TARCEVA (erlotinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Non-Small Cell Lung Cancer (NSCLC)
   Tarceva is indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test receiving first-line, maintenance, or second or greater line treatment after progression following at least one prior chemotherapy regimen.

   Limitations of use:
   a. Safety and efficacy of Tarceva have not been established in patients with NSCLC whose tumors have other EGFR mutations.
   b. Tarceva is not recommended for use in combination with platinum-based chemotherapy.

2. Pancreatic cancer
   Tarceva in combination with gemcitabine is indicated for the first-line treatment of patients with locally advanced, unresectable or metastatic pancreatic cancer.

B. Compendial Uses

1. NSCLC, recurrent, advanced or metastatic sensitizing EGFR mutation-positive
2. Recurrent bone cancer – recurrent chordoma
3. Renal cell carcinoma, relapsed or stage IV disease with non-clear cell histology
4. Recurrent brain metastases from EGFR sensitizing mutation-positive NSCLC
5. Vulvar cancer

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: EGFR mutation testing results (where applicable).

III. CRITERIA FOR INITIAL APPROVAL

A. Non-small cell lung cancer (NSCLC)
Authorization of 12 months may be granted for treatment of recurrent, advanced or metastatic NSCLC (including brain metastases from NSCLC) when the member has sensitizing EGFR mutation-positive disease.

B. Pancreatic cancer
Authorization of 12 months may be granted for treatment of locally advanced, unresectable or metastatic pancreatic cancer.

C. Renal cell carcinoma (RCC)
Authorization of 12 months may be granted for treatment of relapsed or stage IV renal cell carcinoma with non-clear cell histology.

D. Chordoma
Authorization of 12 months may be granted for treatment of recurrent chordoma.

E. Vulvar cancer
Authorization of 12 months may be granted for treatment of vulvar cancer.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced an unacceptable toxicity.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

TASIGNA (nilotinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Adult patients and pediatric patients greater than or equal to 1 year of age with newly diagnosed Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase
   2. Adult patients with chronic phase and accelerated phase Ph+ CML resistant or intolerant to prior therapy that included imatinib
   3. Pediatric patients greater than or equal to 1 year of age with chronic phase Ph+ CML with resistance or intolerance to prior tyrosine-kinase inhibitor (TKI) therapy.

B. Compendial Uses
   1. Primary treatment of advanced phase CML (accelerated phase or blast phase)
   2. Follow-up therapy for CML patients after hematopoietic stem cell transplant (HSCT)
   3. CML patients resistant or intolerant to primary treatment with alternative tyrosine kinase inhibitors (TKIs)
   4. Ph+ acute lymphoblastic leukemia (ALL)
   5. Gastrointestinal stromal tumor (GIST) in patients with disease progression on imatinib, sunitinib or regorafenib

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review:

A. Prior to initiation of therapy for treatment of CML or Ph+ ALL: results of cytogenetic and/or molecular testing for detection of the Ph chromosome or the BCR-ABL gene

B. For members requesting initiation of Tasigna therapy for treatment of CML or ALL after experiencing resistance to prior tyrosine kinase inhibitor (TKI) therapy: results of T315I mutation testing

III. CRITERIA FOR INITIAL APPROVAL

A. Chronic Myeloid Leukemia (CML)

Authorization of 6 months may be granted for treatment of CML that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when any of the following criteria are met:

1. Member has not received prior therapy with a TKI (e.g., bosutinib, dasatinib, imatinib, ponatinib)
2. Member experienced toxicity or intolerance to prior therapy with a TKI
3. Member experienced resistance to prior therapy with a TKI and results of mutational testing are negative for T315I mutation
4. Member has received HSCT for CML

B. Ph+ Acute Lymphoblastic Leukemia (ALL)/Lymphoblastic Lymphoma (LL)
Authorization of 12 months may be granted for treatment of Ph+ ALL or LL that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when any of the following criteria are met:
1. Member has not received prior therapy with a TKI (e.g., bosutinib, dasatinib, imatinib, ponatinib)
2. Member experienced toxicity or intolerance to prior therapy with a TKI
3. Member experienced resistance to prior therapy with a TKI and results of mutational testing are negative for T315I mutation

C. Gastrointestinal stromal tumor (GIST)
Authorization of 12 months may be granted for treatment of GIST who have experienced disease progression on imatinib, sunitinib, or regorafenib.

IV. CONTINUATION OF THERAPY

A. CML
Authorization of 12 months may be granted for treatment of CML that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when any of the following criteria are met:
1. BCR-ABL1 ≤ 10% for members who have been receiving Tasigna for ≤ 12 months
2. No evidence of disease progression for members who have been receiving Tasigna for > 12 months
3. Member has received HSCT

B. Ph+ ALL/LL
Authorization of 12 months may be granted for continued treatment of Ph+ ALL or LL that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing in members who have not experienced disease progression or an unacceptable toxicity.

C. GIST
Authorization of 12 months may be granted for continued treatment of GIST in members who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

TAVALISSE (fostamatinib disodium hexahydrate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

**FDA-Approved Indications**
Treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

**Chronic or persistent immune thrombocytopenia (ITP)**
Authorization of 12 weeks may be granted to members 18 years of age or older with chronic or persistent ITP who meet all of the following criteria:

A. Inadequate response or intolerance to prior therapy such as corticosteroids, immunoglobulins, splenectomy, or thrombopoietin receptor agonists.

B. Untransfused platelet count prior to the initiation of ITP therapy is less than 30x10^9/L OR 30x10^9/L to 50x10^9/L with symptomatic bleeding (e.g., significant mucous membrane bleeding, gastrointestinal bleeding or trauma) or risk factors for bleeding (see Section IV).

III. CONTINUATION OF THERAPY

**Chronic or persistent ITP**

A. Authorization of 12 months may be granted to members 18 years of age or older with current platelet count less than or equal to 200x10^9/L.

B. Authorization of 12 months may be granted to members 18 years of age or older with current platelet count greater than 200 x10^9/L for whom Tavalisse dosing will be adjusted to achieve a platelet count sufficient to avoid clinically important bleeding.

IV. APPENDIX

**Examples of risk factors for bleeding (not all inclusive)**

- Undergoing a medical or dental procedure where blood loss is anticipated
- Comorbidity (e.g., peptic ulcer disease, hypertension)
- Mandated anticoagulation therapy
- Profession (e.g., construction worker) or lifestyle (e.g., plays contact sports) that predisposes patient to trauma
V. REFERENCES

# PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>TAZAROTENE TOPICAL COMBINATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRAND NAME*</td>
<td>DUOBRII (halobetasol propionate and tazarotene)</td>
</tr>
</tbody>
</table>

**Status:** CVS Caremark Criteria  
**Type:** Initial Prior Authorization with Quantity Limit  
Ref # 3062-C

*Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

## FDA-APPROVED INDICATIONS
Duobrii (halobetasol propionate and tazarotene) Lotion, 0.01%/0.045% is indicated for the topical treatment of plaque psoriasis in adults.

## COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:
- The requested drug is being prescribed for the treatment of plaque psoriasis in an adult patient  
  AND  
- The patient experienced an inadequate treatment response or intolerance to a topical corticosteroid

Quantity limits apply.

## RATIONALE
The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Duobrii (halobetasol propionate and tazarotene) Lotion, 0.01%/0.045% is indicated for the topical treatment of plaque psoriasis in adults.

Apply a thin layer of Duobrii Lotion once daily to cover only affected areas. The total dosage should not exceed approximately 50gm per week because of the potential for the drug to suppress the hypothalamic-pituitary-adrenal (HPA) axis.

The American Academy of Dermatology (AAD) Guidelines of Care for the Management of Psoriasis recommends topical corticosteroids as the cornerstone of treatment for the majority of patients with psoriasis, particularly those with limited disease. Topical corticosteroids are available in many strengths and formulations, which allows for versatility of use. In adults, mid- or high-potency agents are generally recommended as initial therapy. Patients with thick, chronic plaques often require treatment with the highest potency corticosteroids. The AAD guidelines also address combination of topical therapies. They state that adding topical corticosteroids to a regimen of tazarotene is an appropriate option owing to the potential irritancy of topical tazarotene. Therefore, a trial of a topical corticosteroid will be required.

The AAD guidelines state in general, it is recommended that more potent agents be used on a short-term basis to allow for response, after which patients should be instructed to use these agents intermittently for long-term management. This strategy may confer less risk of side effects than continuous treatment. Alternatively, patients who require continuous topical treatment should be instructed to use the least potent agent that allows for disease control or be transitioned to a topical agent that is associated with the lowest long-term risk. The safety and efficacy of once daily use of Duobrii Lotion for the treatment of moderate to severe plaque psoriasis were assessed in two prospective, multicenter, randomized, double-blind clinical trials. These trials were conducted in 418 subjects 18 years of age and older.
older with moderate to severe plaque psoriasis that covered a BSA between 3% and 12% excluding the face, scalp, palms, soles, axillae, and intertriginous areas. The AAD states approximately 80% of patients affected with psoriasis have limited disease. Approximately 80% of patients with psoriasis have mild to moderate disease. The severity of psoriasis is defined not only by extent of body surface area (BSA) involvement (<5% being considered mild, 5% to <10% moderate, and >10% severe), but also by involvement of the hands, feet, facial, or genital regions, by which the disease may interfere significantly with activities of daily life. The approval quantity limit will be 100gm per month which is based on the average AAD estimation for up to 20%BSA for acute once daily treatment for two weeks and for maintenance or gradual reduction in therapy, or up to 13%BSA for longer duration of treatment taking into consideration the available package size. The three month limit will be 300gm, which is 3 times the one month limit. Duobrii (halobetasol propionate and tazarotene) Lotion, 0.01%/0.045% is supplied in a 100 gram tube.

The AAD guideline guidance regarding the appropriate amount of topical agents to be applied to affected skin derives from the concept of the fingertip unit which provides a means for patients to more accurately dose their topical medications needed to cover a given body surface area. One fingertip unit is approximately 500mg, which covers approximately 2% BSA.

<table>
<thead>
<tr>
<th>Area to be treated</th>
<th>No. of fingertip units</th>
<th>Approximate body surface area (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scalp</td>
<td>3</td>
<td>6%</td>
</tr>
<tr>
<td>Face and neck</td>
<td>2.5</td>
<td>5%</td>
</tr>
<tr>
<td>One hand (front and back) including fingers</td>
<td>1</td>
<td>2%</td>
</tr>
<tr>
<td>One entire arm including entire hand</td>
<td>4</td>
<td>8%</td>
</tr>
<tr>
<td>Elbows (large plaque)</td>
<td>1</td>
<td>2%</td>
</tr>
<tr>
<td>Both soles</td>
<td>1.5</td>
<td>3%</td>
</tr>
<tr>
<td>One foot (dorsum and sole) including toes</td>
<td>1.5</td>
<td>3%</td>
</tr>
<tr>
<td>One entire leg including entire foot</td>
<td>8</td>
<td>16%</td>
</tr>
<tr>
<td>Buttocks</td>
<td>4</td>
<td>8%</td>
</tr>
<tr>
<td>Knees (large plaque)</td>
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<td>2%</td>
</tr>
<tr>
<td>Trunk (anterior)</td>
<td>8</td>
<td>16%</td>
</tr>
<tr>
<td>Trunk (posterior)</td>
<td>8</td>
<td>16%</td>
</tr>
<tr>
<td>Genitalia</td>
<td>0.5</td>
<td>1%</td>
</tr>
</tbody>
</table>

**Quantity for 1%BSA, suggested AAD estimation**

- **Grams per application**
  - 500mg per application over 2%BSA = 0.25gm per application over 1%BSA
- **Applications per month**
  - For a month supply, at 2 weeks acute daily treatment (14 days) and maintenance twice weekly (or gradual reduction) (6 days) therapy at 1 application per day = (14+6) days x 1 per day = 20 applications per month
  - **Grams per month for 1%BSA**
    - At 0.25gm per application over 1%BSA x 20 applications per month = 0.25gm x 20 = 5gm per 1%BSA per month

**PA Quantity**

- 100gm per month is sufficient for suggested AAD estimation for up to 20%BSA at 2 weeks and maintenance or for at least 13%BSA at longer duration of treatment.
- 100gm per month / 5gm per month over 1%BSA = 20%BSA
- 100gm per month at 0.25gm per application over 1%BSA = 400 applications
- 400 applications over 1%BSA / 20 once daily applications per 2 weeks acute and maintenance = 20%BSA
- 400 applications over 1%BSA / 30 once daily applications per month = 13%BSA

**REFERENCES**


<table>
<thead>
<tr>
<th>CRITERIA FOR APPROVAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Is the requested drug being prescribed for the treatment of plaque psoriasis in an adult patient?</td>
</tr>
<tr>
<td>2. Has the patient experienced an inadequate treatment response or intolerance to a topical corticosteroid?</td>
</tr>
<tr>
<td>3. Does the patient require more than the plan allowance of 100 grams per month?</td>
</tr>
</tbody>
</table>

[RPh Note: If yes, then deny and enter a partial approval for 100 gm/25 days*, 300 gm/75 days*.

Mapping Instructions

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
<th>DENIAL REASONS – DO NOT USE FOR MEDICARE PART D</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Go to 2</td>
<td>Deny</td>
<td>You do not meet the requirements of your plan. Your plan covers the requested drug when it is used for the treatment of plaque psoriasis in an adult patient. Your request has been denied based on the information we have.</td>
</tr>
<tr>
<td>2. Go to 3</td>
<td>Deny</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have tried a topical corticosteroid and it either did not work for you or you cannot use it. Your request has been denied based on the information we have.</td>
</tr>
<tr>
<td>3. Deny</td>
<td>Approve, 12 months, 100 gm/25 days*, 300 gm/75 days*</td>
<td>You do not meet the requirements of your plan. You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 100 grams/month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.</td>
</tr>
</tbody>
</table>

[Short Description: No approvable diagnosis.]

[Short Description: No trial of a generic topical corticosteroid.]

[Short Description: Over max quantity.]

* The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.
SPECIALTY GUIDELINE MANAGEMENT

TECENTRIQ (atezolizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Locally advanced or metastatic urothelial carcinoma
   Tecentriq is indicated for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma who:
   a. Are not eligible for cisplatin-containing chemotherapy, and whose tumors express PD-L1 (PD-L1 stained tumor-infiltrating immune cells [IC] covering >5% of the tumor area), as determined by an FDA-approved test, or
   b. Are not eligible for any platinum-containing chemotherapy regardless of PD-L1 status, or
   c. Have disease progression during or following any platinum-containing chemotherapy, or within 12 months of neoadjuvant or adjuvant chemotherapy.

2. Metastatic non-small cell lung cancer (NSCLC)
   a. Tecentriq is indicated in combination with bevacizumab, paclitaxel, and carboplatin, for the first-line treatment, of adult patients with metastatic non-squamous NSCLC with no EGFR or ALK genomic tumor aberrations.
   b. Tecentriq is indicated for the treatment of adult patients with metastatic NSCLC who have disease progression during or following platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Tecentriq.

3. Unresectable locally advanced or metastatic triple-negative breast cancer (TNBC)
   Tecentriq is indicated in combination with paclitaxel protein-bound for the treatment of adult patients with unresectable locally advanced or metastatic TNBC whose tumors express PD-L1 (PD-L1 stained tumor-infiltrating immune cells [IC] of any intensity covering ≥1% of the tumor area), as determined by an FDA approved test.

4. Small cell lung cancer (SCLC)
   Tecentriq is indicated in combination with carboplatin and etoposide, for the first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC).

B. Compendial Uses

1. Non-small cell lung cancer after progression on or after cytotoxic chemotherapy
2. Negative epidermal growth factor receptor (EGFR), negative anaplastic lymphoma kinase (ALK), negative c-ros oncogene 1 (ROS1) non-squamous non-small cell lung cancer
3. Positive epidermal growth factor receptor (EGFR), positive anaplastic lymphoma kinase (ALK), positive c-ros oncogene 1 (ROS1) non-small cell lung cancer after failure of targeted therapy
All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Urothelial carcinoma
Authorization of 12 months may be granted for treatment of locally advanced or metastatic urothelial carcinoma when any of the following criteria are met:
1. Member is not eligible for cisplatin-containing chemotherapy, and the member’s tumor expresses PD-L1 (PD-L1 stained tumor-infiltrating immune cells [IC] covering ≥5% of the tumor area), as determined by an FDA-approved test, or
2. Member is not eligible for any platinum-containing chemotherapy regardless of PD-L1 status, or
3. The disease has progressed during or following platinum-containing chemotherapy, or within 12 months of neoadjuvant or adjuvant chemotherapy.

B. Non-small cell lung cancer (NSCLC)
Authorization of 12 months may be granted for treatment of metastatic NSCLC when any of the following criteria are met:
1. The disease has progressed during or following cytotoxic chemotherapy.
2. Member has positive epidermal growth factor receptor (EGFR) mutation, positive anaplastic lymphoma kinase (ALK), or positive c-ros oncogene 1 (ROS1) gene rearrangement who have had disease progression on targeted FDA-approved therapy (e.g., erlotinib, afatinib, gefitinib, crizotinib, ceritinib) prior to receiving Tecentriq.
3. Member has non-squamous histology and is negative for epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase (ALK), or c-ros oncogene 1 (ROS1) mutation.

C. Breast cancer
Authorization of 12 months may be granted for treatment of breast cancer when any of the following criteria are met:
1. The diagnosis of breast cancer is confirmed by the cancer cells testing negative for ALL of the following receptors:
   a. human epidermal growth factor receptor 2 (HER-2)
   b. estrogen
   c. progesterone
2. Tumors must express programmed death ligand 1 (PD-L1) (i.e., PD-L1 stained tumor-infiltrating immune cells [IC] of any intensity covering ≥ 1 percent of the tumor area), as determined by an FDA approved test.
3. Tecentriq will be used in combination with protein-bound paclitaxel.

D. Small cell lung cancer (SCLC)
Authorization of 12 months may be granted for treatment of small cell lung cancer when both of the following criteria are met:
1. Patient has extensive-stage disease.
2. Tecentriq will be used in combination with etoposide and carboplatin.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.
IV. REFERENCE
SPECIALTY GUIDELINE MANAGEMENT

TECFIDERÁ (dimethyl fumarate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Tecfidera is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease and active secondary progressive disease, in adults.

All other indications are considered experimental/investigational and are not covered benefits.

II. CRITERIA FOR INITIAL APPROVAL

A. Relapsing forms of multiple sclerosis
Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

B. Clinically isolated syndrome
Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome.

III. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted for members who are experiencing disease stability or improvement while receiving Tecfidera.

IV. OTHER CRITERIA

Members will not use Tecfidera concomitantly with other medications used for the treatment of multiple sclerosis, excluding Ampyra.

V. REFERENCE

SPECIALTY GUIDELINE MANAGEMENT

TECHNIVIE (ombitasvir/paritaprevir/ritonavir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Technivie is indicated in combination with ribavirin for the treatment of patients with genotype 4 chronic hepatitis C virus (HCV) infection without cirrhosis or with compensated cirrhosis.

All other indications are considered experimental/investigational and are not a covered benefit.

II. EXCLUSIONS

Coverage will not be provided for members with decompensated cirrhosis/moderate or severe hepatic impairment (Child Turcotte Pugh Class B or C)

Note: When the requested drug is being used in a combination therapy regimen, exclusions to the other antiviral drugs also apply.

III. CRITERIA FOR APPROVAL

A. Chronic hepatitis C virus infection, in combination with ribavirin (RBV)
   Genotype 4 infection
   Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are either of the following:
   1. Treatment-naïve
   2. Failed prior treatment with peginterferon alfa and RBV

B. Chronic hepatitis C virus infection, without RBV
   Genotype 4 infection
   Authorization of up to 12 weeks total may be granted for members without cirrhosis who meet all of the following criteria:
   1. Treatment-naïve
   2. Member has intolerance to RBV, has documented anemia (baseline hemoglobin below 10 g/dL) or RBV ineligibility (see Section V for ribavirin ineligibility)

C. HCV and HIV coinfection
   Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A or B above are met.

IV. CONTINUATION OF THERAPY
All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. APPENDIX: RIBAVIRIN INELIGIBILITY

RBV ineligibility is defined as one or more of the below:
- Pregnant female or male whose female partner is pregnant
- Hemoglobinopathy
- Coadministration with didanosine
- History of significant or unstable cardiac disease

VI. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

TEGSEDI (inotersen)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Tegsedi is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Testing or analysis confirming a mutation of the TTR gene
B. Medical record documentation confirming the member demonstrates signs and symptoms of polyneuropathy and an improvement in these signs and symptoms since starting therapy for continuation

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a neurologist, geneticist, or physician specializing in the treatment of amyloidosis.

IV. CRITERIA FOR INITIAL APPROVAL

Polyneuropathy of Hereditary Transthyretin-mediated Amyloidosis

Authorization of 12 months may be granted for treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis (also called transthyretin-type familial amyloid polyneuropathy [ATTR-FAP]) when all of the following criteria are met:

A. The diagnosis is confirmed by detection of a mutation of the TTR gene.
B. Member exhibits clinical manifestations of ATTR-FAP (e.g., amyloid deposition in biopsy specimens, TTR protein variants in serum, progressive peripheral sensory-motor polyneuropathy).
C. The member is not a liver transplant recipient.
D. The requested medication will not be used in combination with patisiran (Onpattro) or tafamidis.

V. CONTINUATION OF THERAPY
Authorization of 12 months may be granted for the continued treatment of ATTR-FAP when all of the following criteria are met:
A. The member must have met all initial authorization criteria.
B. The member must have demonstrated a beneficial response to treatment with Tegsedi therapy compared to baseline (e.g., improvement of neuropathy severity and rate of disease progression as demonstrated by the modified Neuropathy Impairment Scale+7 (mNIS+7) composite score, the Norfolk Quality of Life-Diabetic Neuropathy (QoL-DN) total score, polyneuropathy disability (PND) score, FAP disease stage, manual grip strength). Documentation from the medical record must be provided.

VI. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

Temodar (temozolomide)
temozolomide (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Newly Diagnosed Glioblastoma Multiforme
Temodar is indicated for the treatment of adult patients with newly diagnosed glioblastoma multiforme concomitantly with radiotherapy and then as maintenance treatment.

2. Refractory Anaplastic Astrocytoma
Temodar is indicated for the treatment of adult patients with refractory anaplastic astrocytoma, i.e., patients who have experienced disease progression on a drug regimen containing nitrosourea and procarbazine.

B. Compendial Uses

1. Central nervous system (CNS) cancer
2. Ewing sarcoma
3. Neuroendocrine tumors of pancreas, gastrointestinal tract, lung, and thymus
4. Poorly differentiated (high grade) neuroendocrine tumors/large or small cell carcinoma
5. Pheochromocytoma/paraganglioma
6. Melanoma
7. Mycosis fungoides/Sézary syndrome
8. Small cell lung cancer
9. Soft tissue sarcoma
10. Uterine sarcoma
11. Primary cutaneous anaplastic large cell lymphoma (ALCL)

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Central nervous system (CNS) cancer
Authorization of 12 months may be granted for treatment of CNS cancers.

B. Ewing sarcoma
Authorization of 12 months may be granted for treatment of Ewing sarcoma.

C. Neuroendocrine tumors of pancreas, gastrointestinal tract, lung, and thymus
Authorization of 12 months may be granted for treatment of neuroendocrine tumors of pancreas, gastrointestinal tract, lung, or thymus.

D. Poorly differentiated (high grade) neuroendocrine tumors/large or small cell carcinoma
Authorization of 12 months may be granted for treatment of poorly differentiated (high grade) neuroendocrine tumors or large or small cell carcinoma.

E. Pheochromocytoma/paraganglioma²
Authorization of 12 months may be granted for treatment of pheochromocytoma or paraganglioma.

F. Melanoma²
Authorization of 12 months may be granted for treatment of metastatic or unresectable melanoma.

G. Mycosis fungoides/Sezary syndrome²
Authorization of 12 months may be granted for treatment of mycosis fungoides/Sezary syndrome.

H. Small cell lung cancer (SCLC)²
Authorization of 12 months may be granted for treatment of SCLC.

I. Soft tissue sarcoma (STS)²,4
Authorization of 12 months may be granted for treatment of STS.

J. Uterine sarcoma²
Authorization of 12 months may be granted for treatment of uterine sarcoma.

K. Primary cutaneous anaplastic large cell lymphoma (ALCL)²
Authorization of 12 months may be granted for treatment of primary cutaneous ALCL.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>BRAND NAME* (generic)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DEPO-TESTOSTERONE (testosterone cypionate injection)</td>
</tr>
</tbody>
</table>

**Status:** CVS Caremark Criteria  
**Type:** Initial Prior Authorization  
**Ref #** 1371-A

*Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

**FDA-APPROVED INDICATIONS**

Depo-Testosterone Injection is indicated for replacement therapy in the male in conditions associated with symptoms of deficiency or absence of endogenous testosterone:

- Primary hypogonadism (congenital or acquired) - testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, or orchiectomy.
- Hypogonadotropic hypogonadism (congenital or acquired) - gonadotropin or LHRH deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation.

Safety and efficacy of Depo-Testosterone in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.

**COVERAGE CRITERIA**

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for primary or hypogonadotropic hypogonadism [Note: Safety and efficacy of testosterone products in patients with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.]
  AND
  - Before the start of testosterone therapy, the patient has at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values OR
  - For continuation of testosterone therapy: before the patient started testosterone therapy, the patient had a confirmed low testosterone level according to current practice guidelines or your standard lab reference values

**RATIONALE**

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Depo-Testosterone (testosterone cypionate) is indicated for replacement therapy in males in conditions associated with symptoms of deficiency or absence of endogenous testosterone: congenital or acquired primary hypogonadism (testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, or orchiectomy), or congenital or acquired hypogonadotropic hypogonadism (gonadotropin or luteinizing hormone-releasing hormone [LHRH] deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation). Safety and efficacy of Depo-Testosterone in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.1-3

A testosterone determination, in conjunction with a free testosterone or sex hormone-binding globulin level, is the threshold test in the evaluation of suspected male hypogonadism (serum total testosterone levels less than 300 ng/dL). Testosterone levels should be determined in the morning, and studies should be repeated in patients with subnormal
levels. The normative ranges for total and free testosterone levels in healthy young men vary among laboratories and assays. In some laboratories, the lower limit of the normal range for total testosterone level in healthy young men is 280-300 ng/dL and for serum free testosterone level is 5–9 pg/mL. The clinicians should use the lower limit of normal range for healthy young men established in their laboratory.4,5 For initial therapy, testosterone will be approved for patients with at least two confirmed low testosterone levels according to current practice guidelines or standard lab reference values. If the patient is already on testosterone therapy and did not get a repeat testosterone level before starting therapy, it would be inappropriate for the patient to stop treatment to get a repeat testosterone level. For continuation of therapy, one low testosterone level is required before the patient started testosterone therapy.

REFERENCES

Written by: UM Development (MG)
Date: 05/2003
Revised: (NB) 01/2005, (MG) 02/2006; (NB) 02/2007(2); (AM) 01/2008, 12/2008; (MS) 11/2009, 11/2010, (TM) 11/2011, 10/2012 (extended duration); (PL) 11/2012, (SE) 04/2013 (created separate Med-D depo-testosterone document), (PL) 11/2013,(SE) 04/2014 (rephrased diagnosis question); (CF/JH) 11/2014, 02/2015 (updated testosterone level question), (LN) 04/2015 (added denial reasons); (CF/JH) 11/2015; (JH) 05/2016 (removed TGC coverage); (CF/JH) 11/2016; (KC) 11/2017 (no clinical changes), 10/2018 (no clinical changes), 08/2019 (removed "male" from lab questions)

CRITERIA FOR APPROVAL

1. Is the requested drug being prescribed for primary or hypogonadotropic hypogonadism? Yes No
   [Note: Safety and efficacy of testosterone products in patients with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.]
2. Is this request for a continuation of testosterone therapy? Yes No
   [If no, then skip to question 4.]
3. Before the patient started testosterone therapy, did the patient have a confirmed low testosterone level according to current practice guidelines or your standard lab reference values? Yes No
   [No further questions.]
4. Does the patient have at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values? Yes No
### Mapping Instructions

<table>
<thead>
<tr>
<th>Yes</th>
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</thead>
<tbody>
<tr>
<td>1. Go to 2</td>
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</tr>
<tr>
<td>2. Go to 3</td>
<td>Go to 4</td>
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<tr>
<td>3. Approve, 12 months</td>
<td>Deny</td>
</tr>
<tr>
<td>4. Approve, 12 months</td>
<td>Deny</td>
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</table>
PRIOR AUTHORIZATION CRITERIA

DRUG CLASS  TESTOSTERONE PRODUCTS - INJECTABLE

BRAND NAME* (generic)

DEPO-TESTOSTERONE (testosterone cypionate injection)

Status: CVS Caremark Criteria  MDC-2
Type: Initial Prior Authorization  Ref # 976-A

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS
Depo-Testosterone Injection is indicated for replacement therapy in the male in conditions associated with symptoms of deficiency or absence of endogenous testosterone:
Primary hypogonadism (congenital or acquired) - testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, or orchiectomy.
Hypogonadotropic hypogonadism (congenital or acquired) - gonadotropin or LHRH deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation.

Limitations of Use
Safety and efficacy of Depo-Testosterone in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.

Compendial Uses
Gender Dysphoria in transgender male patients 2,3,6-9

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:
• The requested drug is being prescribed for primary or hypogonadotropic hypogonadism [Note: Safety and efficacy of testosterone products in patients with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.]
  AND
  o Before the start of testosterone therapy, the patient has at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values OR
  o For continuation of testosterone therapy: before the patient started testosterone therapy, the patient had a confirmed low testosterone level according to current practice guidelines or your standard lab reference values

OR
• The requested drug is being prescribed for gender dysphoria in a patient who is able to make an informed decision to engage in hormone therapy

RATIONALE
These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.
The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Depo-Testosterone is indicated for replacement therapy in males in conditions associated with symptoms of deficiency or absence of endogenous testosterone: congenital or acquired primary hypogonadism (testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, or orchiectomy), or congenital or acquired hypogonadotropic hypogonadism (gonadotropin or luteinizing hormone-releasing hormone [LHRH] deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation). Safety and efficacy of Depo-Testosterone in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.1-3

A testosterone determination, in conjunction with a free testosterone or sex hormone-binding globulin level, is the threshold test in the evaluation of suspected male hypogonadism (serum total testosterone levels less than 300 ng/dL [nanograms per deciliter]). Testosterone levels should be determined in the morning, and studies should be repeated in patients with subnormal levels. The normative ranges for total and free testosterone levels in healthy young men vary among laboratories and assays. In some laboratories, the lower limit of the normal range for total testosterone level in healthy young men is 280-300 ng/dL and for serum free testosterone level is 5–9 pg/mL (picograms per milliliter). Clinicians should use the lower limit of normal range for healthy young men established in their laboratory.4,5 For initial therapy, testosterone will be approved for patients with at least two confirmed low testosterone levels according to current practice guidelines or standard lab reference values. If the patient is already on testosterone therapy and did not get a repeat testosterone level before starting therapy, it would be inappropriate for the patient to stop treatment to get a repeat testosterone level. For continuation of therapy, one low testosterone level is required before the patient started testosterone therapy.

Depo-Testosterone (testosterone cypionate) has a compendial use for gender dysphoria in transgender male (female-to-male) patients.2-3, 6-9

Transgender persons seeking to develop the physical characteristics of the desired gender require a safe, effective hormone regimen that will suppress endogenous hormone secretion determined by the person’s genetic/biologic sex and maintain sex hormone levels within the normal range for the person’s desired gender. The two major goals of hormonal therapy are to reduce endogenous hormone levels and, thereby, the secondary sex characteristics of the individual’s biological/genetic sex and to replace endogenous sex hormone levels with those of the reassigned sex. The Endocrine Society suggests that pubertal development of the desired opposite sex be initiated at about the age of 16 years, using a gradually increasing dose schedule of cross-sex steroids. However, the Endocrine Society Guidelines also state that identifying an age at which pubertal development is initiated can be difficult and may depend on several factors (such as the age when pubertal suppression was begun, medications used to initiate pubertal suppression, and relative risks of prolonged pubertal suppression), and the goal is to start the process at a time when the individual will be able to make informed, mature decisions to engage in the therapy. Some patients may advance to Tanner stage 2 of pubertal development at an early age (such as 9 or 10) and using pubertal suppression therapy for 6 or 7 years may be deemed inappropriate. Medical professionals involved in the patient’s care should be involved in assessing whether the patient is ready to make the decision to begin hormone therapy and pubertal development.6 Therefore, individuals who are able to make an informed decision to engage in hormone therapy will be approved.

For transgender male persons, regimens to change secondary sex characteristics follow the general principle of hormone replacement treatment of male hypogonadism. Either parenteral or transdermal preparations can be used to achieve testosterone values in the normal male range (320-1000 ng/dL).6 The agent primarily used for endocrine treatment of transgender male patients is testosterone. When determining the appropriate method of testosterone delivery, many considerations should be taken into account. The most well-described formulation of testosterone therapy used to treat transgender male patients is intramuscular injection of testosterone esters (cypionate or enanthate).7

REFERENCES

Written by: UM Development (MG)
Date: 05/2003
Revised: (NB) 01/2005, (MG) 02/2006; (NB) 02/2007(2); (AM) 01/2008, 12/2008; (MS) 11/2009, 11/2010, (TM) 11/2011, 10/2012 (extended duration); (PL) 11/2012, (SE) 04/2013 (created separate Med-D depo-testosterone document), (PL) 11/2013,(SE) 04/2014 (rephrased diagnosis question); (CF/JH) 11/2014, 02/2015 (updated testosterone level question), (LN) 04/2015 (added denial reasons); (CF/JH) 11/2015, (SE) 06/2016 (created separate Med D); (CF/JH) 02/2017; (KC) 02/2018, 02/2019 (no clinical changes), 06/2019 (updated questions)

### CRITERIA FOR APPROVAL

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<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
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<tbody>
<tr>
<td>1  Is the requested drug being prescribed for primary or hypogonadotropic hypogonadism? [Note: Safety and efficacy of testosterone products in patients with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.] [If no, then skip to question 5.]</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>2  Is this request for a continuation of testosterone therapy? [If no, then skip to question 4.]</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>3  Before the patient started testosterone therapy, did the patient have a confirmed low testosterone level according to current practice guidelines or your standard lab reference values? [No further questions.]</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>4  Does the patient have at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values? [No further questions.]</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>5  Is the requested drug being prescribed for gender dysphoria in a patient who is able to make an informed decision to engage in hormone therapy?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
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</tr>
<tr>
<td>1</td>
<td>Go to 2</td>
<td>Go to 5</td>
</tr>
<tr>
<td>2</td>
<td>Go to 3</td>
<td>Go to 4</td>
</tr>
</tbody>
</table>
| 3 | Approve, 12 months | Deny                   | You do not meet the requirements of your plan. Your plan covers this drug when you have had a test that showed low testosterone levels before you started testosterone therapy. 
Your request has been denied based on the information we have.  
[Short Description: No confirmation of diagnosis (tests, labs, etc.)] |
| 4 | Approve, 12 months | Deny                   | You do not meet the requirements of your plan. Your plan covers this drug when you have had two tests that showed low testosterone levels. Your request has been denied based on the information we have.  
[Short Description: No confirmation of diagnosis (tests, labs, etc.)] |
| 5 | Approve, 12 months | Deny                   | You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions:  
- You have primary or hypogonadotropic hypogonadism  
- You have gender dysphoria and you can make an informed decision to use this drug  
Your request has been denied based on the information we have.  
[Short Description: No approvable diagnosis] |
PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>TESTOSTERONE PRODUCTS – ORAL</th>
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<tbody>
<tr>
<td>BRAND NAME*</td>
<td>JATENZO (testosterone undecanoate oral)</td>
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<td>(generic)</td>
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**Status:** CVS Caremark Criteria  
**Type:** Initial Prior Authorization  
**Ref # 3059-A**

*Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

**FDA-APPROVED INDICATIONS**

Jatenzo is an androgen indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone:

- Primary hypogonadism (congenital or acquired) - testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchietomy, Klinefelter Syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations and gonadotropins (FSH, LH) above the normal range.
- Hypogonadotropic hypogonadism (congenital or acquired) - gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations but have gonadotropins in the normal or low range.

**Limitations of Use**

Safety and efficacy of Jatenzo in males less than 18 years old have not been established.

**COVERAGE CRITERIA**

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for primary or hypogonadotropic hypogonadism [Note: Safety and efficacy of testosterone products in patients with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.] AND
  - Before the start of testosterone therapy, the patient has at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values OR
  - For continuation of testosterone therapy: before the patient started testosterone therapy, the patient had a confirmed low testosterone level according to current practice guidelines or your standard lab reference values

**RATIONALE**

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Jatenzo is indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone: congenital or acquired primary hypogonadism (testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchietomy, Klinefelter Syndrome, chemotherapy, or toxic damage from alcohol or heavy metals), congenital or acquired hypogonadotropic hypogonadism (gonadotropin or luteinizing hormone-releasing hormone [LHRH] deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation). Safety and efficacy of topical, buccal, and nasal testosterone products in men with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.
The safety and efficacy of Jatenzo was evaluated in 166 adult hypogonadal males in an open-label study of approximately 4 months duration. The primary endpoint was the percentage of patients with mean plasma total testosterone concentration over 24 hours within the normal eugonadal range on the final pharmacokinetics visit of the study. 145 (87%) of the 166 hypogonadal men who received Jatenzo had a mean total testosterone concentration within the normal eugonadal range at the end of treatment.

A testosterone determination, in conjunction with a free testosterone or sex hormone-binding globulin level, is the threshold test in the evaluation of suspected male hypogonadism (serum total testosterone levels less than 300 ng/dL [nanograms per deciliter]). Testosterone levels should be determined in the morning, and studies should be repeated in patients with subnormal levels. The normative ranges for total and free testosterone levels in healthy young men vary among laboratories and assays. In some laboratories, the lower limit of the normal range for total testosterone level in healthy young men is 280-300 ng/dL and for serum free testosterone level is 5–9 pg/mL (picograms per milliliter). Clinicians should use the lower limit of normal range for healthy young men established in their laboratory. For initial therapy, testosterone will be approved for patients with at least two confirmed low testosterone levels according to current practice guidelines or standard lab reference values. If the patient is already on testosterone therapy and did not get a repeat testosterone level before starting therapy, it would be inappropriate for the patient to stop treatment to get a repeat testosterone level. For continuation of therapy, one low testosterone level is required before the patient started testosterone therapy.

REFERENCES

CRITERIA FOR APPROVAL

<p>| | | | | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>Is the requested drug being prescribed for primary or hypogonadotropic hypogonadism?</td>
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<td>No</td>
<td></td>
<td></td>
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<td></td>
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<td>[Note: Safety and efficacy of testosterone products in patients with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.]</td>
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<td>Is this request for a continuation of testosterone therapy?</td>
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<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>[If no, then skip to question 4.]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Before the patient started testosterone therapy, did the patient have a confirmed low testosterone level according to current practice guidelines or your standard lab reference values?</td>
<td>Yes</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>[No further questions.]</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
4. Does the patient have at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values?  
[No further questions.]

<table>
<thead>
<tr>
<th>Mapping Instructions</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Go to 2</td>
<td>Deny</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have primary or hypogonadotropic hypogonadism. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]</td>
</tr>
<tr>
<td>2. Go to 3</td>
<td>Go to 4</td>
<td></td>
</tr>
<tr>
<td>3. Approve, 12 months</td>
<td>Deny</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have had a test that showed low testosterone levels before you started testosterone therapy. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (tests, labs, etc.)]</td>
</tr>
<tr>
<td>4. Approve, 12 months</td>
<td>Deny</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have had two tests that showed low testosterone levels. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (tests, labs, etc.)]</td>
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PRIOR AUTHORIZATION CRITERIA

<table>
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<tr>
<th>DRUG CLASS</th>
<th>TESTOSTERONE PRODUCTS – ORAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRAND NAME*</td>
<td>(generic)</td>
</tr>
<tr>
<td>JATENZO</td>
<td>(testosterone undecanoate oral)</td>
</tr>
</tbody>
</table>

Status: CVS Caremark Criteria  
Type: Initial Prior Authorization  
Ref # 3060-A

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Jatenzo is an androgen indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone:
Primary hypogonadism (congenital or acquired) - testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter Syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations and gonadotropins (FSH, LH) above the normal range.
Hypogonadotropic hypogonadism (congenital or acquired) - gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations but have gonadotropins in the normal or low range.

Limitations of Use

Safety and efficacy of Jatenzo in males less than 18 years old have not been established.

Compendial Uses

Gender Dysphoria3,6-9

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:
- The requested drug is being prescribed for primary or hypogonadotropic hypogonadism [Note: Safety and efficacy of testosterone products in patients with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.]
  AND
  o Before the start of testosterone therapy, the patient has at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values OR
  o For continuation of testosterone therapy: before the patient started testosterone therapy, the patient had a confirmed low testosterone level according to current practice guidelines or your standard lab reference values

OR
- The requested drug is being prescribed for gender dysphoria in a patient who is able to make an informed decision to engage in hormone therapy

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Jatenzo is indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone: congenital or
acquired primary hypogonadism (testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchietomy, Klinefelter Syndrome, chemotherapy, or toxic damage from alcohol or heavy metals), congenital or acquired hypogonadotropic hypogonadism (gonadotropin or luteinizing hormone-releasing hormone [LHRH] deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation). Safety and efficacy of topical, buccal, and nasal testosterone products in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.

The safety and efficacy of Jatenzo was evaluated in 166 adult hypogonadal males in an open-label study of approximately 4 months duration. The primary endpoint was the percentage of patients with mean plasma total testosterone concentration over 24 hours within the normal eugonadal range on the final pharmacokinetics visit of the study. 145 (87%) of the 166 hypogonadal men who received Jatenzo had a mean total testosterone concentration within the normal eugonadal range at the end of treatment.

A testosterone determination, in conjunction with a free testosterone or sex hormone-binding globulin level, is the threshold test in the evaluation of suspected male hypogonadism (serum total testosterone levels less than 300 ng/dL [nanograms per deciliter]). Testosterone levels should be determined in the morning, and studies should be repeated in patients with subnormal levels. The normative ranges for total and free testosterone levels in healthy young men vary among laboratories and assays. In some laboratories, the lower limit of the normal range for total testosterone level in healthy young men is 280-300 ng/dL and for serum free testosterone level is 5–9 pg/mL (picograms per milliliter). Clinicians should use the lower limit of normal range for healthy young men established in their laboratory. For initial therapy, testosterone will be approved for patients with at least two confirmed low testosterone levels according to current practice guidelines or standard lab reference values. If the patient is already on testosterone therapy and did not get a repeat testosterone level before starting therapy, it would be inappropriate for the patient to stop treatment to get a repeat testosterone level. For continuation of therapy, one low testosterone level is required before the patient started testosterone therapy.

Jatenzo has a compendial use for gender dysphoria in transgender male (female-to-male) patients.

Transgender persons seeking to develop the physical characteristics of the desired gender require a safe, effective hormone regimen that will suppress endogenous hormone secretion determined by the person’s genetic/biologic sex and maintain sex hormone levels within the normal range for the person’s desired gender. The two major goals of hormonal therapy are to reduce endogenous hormone levels and, thereby, the secondary sex characteristics of the individual’s biological/genetic sex and to replace endogenous sex hormone levels with those of the reassigned sex. The Endocrine Society suggests that pubertal development of the desired opposite sex be initiated at about the age of 16 years, using a gradually increasing dose schedule of cross-sex steroids. However, the Endocrine Society Guidelines also state that identifying an age at which pubertal development is initiated can be difficult and may depend on several factors (such as the age when pubertal suppression was begun, medications used to initiate pubertal suppression, and relative risks of prolonged pubertal suppression), and the goal is to start the process at a time when the individual will be able to make informed, mature decisions to engage in the therapy. Some patients may advance to Tanner stage 2 of pubertal development at an early age (such as 9 or 10) and using pubertal suppression therapy for 6 or 7 years may be deemed inappropriate. Medical professionals involved in the patient’s care should be involved in assessing whether the patient is ready to make the decision to begin hormone therapy and pubertal development. Therefore, individuals who are able to make an informed decision to engage in hormone therapy will be approved.

For transgender male (female-to-male) persons, regimens to change secondary sex characteristics follow the general principle of hormone replacement treatment of male hypogonadism. Testosterone generally can be given orally, transdermally, or parenterally (IM) to achieve testosterone values in the normal male range (320-1000 ng/dL). The agent primarily used for endocrine treatment of transgender male patients is testosterone. When determining the appropriate method of testosterone delivery, many considerations should be taken into account. The most well-described formulation of testosterone therapy used to treat transgender male patients is intramuscular injection of testosterone esters (cypionate or enanthate). Because intramuscular testosterone cypionate or enanthate is often administered every 2-4 weeks, some patients may notice a cyclic variation in effects as well as more time outside the normal physiologic levels. Transdermal testosterone has been shown to provide less variation in serum testosterone levels compared with injectable preparations. Testosterone administered transdermally more closely mimics physiologic testosterone levels. However, transdermal preparations achieve low-normal ranges of testosterone levels in hypogonadal men, which may translate to a lessened change in physical appearance and virilization in the transgender male patient.
Testosterone undecanoate formulations available outside the United States result in lower serum testosterone levels than nonoral preparations. However, studies for Jatenzo indicate that it achieves normal serum testosterone levels in hypogonadal patients, indicating that normal levels can be achieved for transgender patients.

REFERENCES

Written by: UM Development (KC)
Date Written: 04/2019
Revised: (KC) 06/2019 (updated gender dysphoria question)
Reviewed: Medical Affairs: (GAD) 05/2019; (ME) 07/2019
External Review: 06/2019

CRITERIA FOR APPROVAL

1. Is the requested drug being prescribed for primary or hypogonadotropic hypogonadism? [Note: Safety and efficacy of testosterone products in patients with “age-related hypogonadism” (also referred to as "late-onset hypogonadism") have not been established.] Yes No
   [If no, then skip to question 5.]

2. Is this request for a continuation of testosterone therapy? Yes No
   [If no, then skip to question 4.]

3. Before the patient started testosterone therapy, did the patient have a confirmed low testosterone level according to current practice guidelines or your standard lab reference values? Yes No
   [No further questions.]

4. Does the patient have at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values? Yes No
   [No further questions.]
5 Is the requested drug being prescribed for gender dysphoria in a patient who is able to make an informed decision to engage in hormone therapy?  

<table>
<thead>
<tr>
<th>Mapping Instructions</th>
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</thead>
<tbody>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>1. Go to 2</td>
</tr>
<tr>
<td>2. Go to 3</td>
</tr>
<tr>
<td>3. Approve, 12 months</td>
</tr>
<tr>
<td>4. Approve, 12 months</td>
</tr>
</tbody>
</table>
| 5. Approve, 12 months | Deny | You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions:  
- You have primary or hypogonadotrophic hypogonadism  
- You have gender dysphoria and you can make an informed decision to use this drug  
Your request has been denied based on the information we have. [Short Description: No approvable diagnosis] |
# Prior Authorization Criteria

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Testosterone Products – Oral</th>
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<tr>
<td>Brand Name*</td>
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<tr>
<td>Android (methyltestosterone oral capsule)</td>
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</tr>
<tr>
<td>Androxy (fluoxymesterone oral tablet)</td>
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<tr>
<td>Methitest (methyltestosterone oral tablet)</td>
<td></td>
</tr>
<tr>
<td>Testred (methyltestosterone oral capsule)</td>
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**Status:** CVS Caremark Criteria  
**Type:** Initial Prior Authorization  
**Ref #:** 2817-A

*Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

## FDA-Approved Indications

**Males**  
Androgens are indicated for replacement therapy in conditions associated with deficiency or absence of endogenous testosterone:  
- Primary hypogonadism (congenital or acquired) - testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, or orchietomy.  
- Hypogonadotropic hypogonadism (congenital or acquired) - gonadotropin or LHRH deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation. (Appropriate adrenal cortical and thyroid hormone replacement therapy are still necessary, however, and are actually of primary importance.)

If the above conditions occur prior to puberty, androgen replacement therapy will be needed during the adolescent years for development of secondary sexual characteristics. Prolonged androgen treatment will be required to maintain sexual characteristics in these and other males who develop testosterone deficiency after puberty. Safety and efficacy of oral testosterone in men with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.

Androgens may be used to stimulate puberty in carefully selected males with clearly delayed puberty. These patients usually have a familial pattern of delayed puberty that is not secondary to a pathological disorder; puberty is expected to occur spontaneously at a relatively late date. Brief treatment with conservative doses may occasionally be justified in these patients if they do not respond to psychological support. The potential adverse effect on bone maturation should be discussed with the patient and parents prior to androgen administration. An X-ray of the hand and wrist to determine bone age should be obtained every 6 months to assess the effect of treatment on the epiphyseal centers.

**Females**  
Androgens may be used secondarily in women with advancing inoperable metastatic (skeletal) mammary cancer who are 1 to 5 years postmenopausal. Primary goals of therapy in these women include ablation of the ovaries. Other methods of countering estrogen activity are adrenalectomy, hypophysectomy, and/or anti-estrogen therapy. This treatment has also been used in premenopausal women with breast cancer who have benefited from oophorectomy and are considered...
to have a hormone-responsive tumor. Judgment concerning androgen therapy should be made by an oncologist with expertise in this field.

**COVERAGE CRITERIA**
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for primary or hypogonadotropic hypogonadism [Note: Safety and efficacy of testosterone products in patients with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.]

  **AND**

  - Before the start of testosterone therapy, the patient has at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values **OR**
  - For continuation of testosterone therapy: before the patient started testosterone therapy, the patient had a confirmed low testosterone level according to current practice guidelines or your standard lab reference values **OR**
  - The requested drug is being prescribed for inoperable metastatic breast cancer in a patient who is 1 to 5 years postmenopausal **OR**
  - The requested drug is being prescribed for a premenopausal patient with breast cancer who has benefited from oophorectomy and is considered to have a hormone-responsive tumor **OR**
  - The requested drug is being prescribed for delayed puberty

**RATIONALE**
The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. In males, oral androgens are indicated for replacement therapy in conditions associated with a deficiency or absence of endogenous testosterone: primary hypogonadism (testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, or orchiectomy), hypogonadotropic hypogonadism (gonadotropin or luteinizing hormone-releasing hormone [LHRH] deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation), and delayed puberty. Safety and efficacy of oral testosterone in men with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established. 1-6

A testosterone determination, in conjunction with a free testosterone or sex hormone-binding globulin level, is the threshold test in the evaluation of suspected male hypogonadism (serum total testosterone levels less than 300 ng/dL). Testosterone levels should be determined in the morning, and studies should be repeated in patients with subnormal levels. The normative ranges for total and free testosterone levels in healthy young men vary among laboratories and assays. In some laboratories, the lower limit of the normal range for total testosterone level in healthy young men is 280-300 ng/dL and for serum free testosterone level is 5–9 pg/mL. The clinicians should use the lower limit of normal range for healthy young men established in their laboratory.7,8 For initial therapy, testosterone will be approved for patients with at least two confirmed low testosterone levels according to current practice guidelines or standard lab reference values. If the patient is already on testosterone therapy and did not get a repeat testosterone level before starting therapy, it would be inappropriate for the patient to stop treatment to get a repeat testosterone level. For continuation of therapy, one low testosterone level is required before the patient started testosterone therapy.

Oral androgens may be used secondarily in women with advancing inoperable metastatic (skeletal) mammary cancer who are one to five years postmenopausal. Primary goals of therapy in these women include ablation of the ovaries. Other methods of counteracting estrogen activity are adrenalectomy, hypophysectomy, and/or anti-estrogen therapy.1-6

This treatment has also been used in premenopausal women with breast cancer who have benefited from oophorectomy and are considered to have a hormone-responsive tumor. Judgment concerning androgen therapy should be made by an oncologist with expertise in this field.1-6
Oral androgens may be used to stimulate puberty in carefully selected males with clearly delayed puberty. Brief treatment with conservative doses may occasionally be justified in these patients if they do not respond to psychological support.¹⁻⁵

**REFERENCES**


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**CRITERIA FOR APPROVAL**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>1</td>
<td>Is the requested drug being prescribed for primary or hypogonadotropic hypogonadism?</td>
</tr>
<tr>
<td></td>
<td>Yes No</td>
</tr>
<tr>
<td></td>
<td>[Note: Safety and efficacy of testosterone products in patients with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.]</td>
</tr>
<tr>
<td></td>
<td>[If no, then skip to question 5.]</td>
</tr>
<tr>
<td>2</td>
<td>Is this request for a continuation of testosterone therapy?</td>
</tr>
<tr>
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<td>Yes No</td>
</tr>
<tr>
<td></td>
<td>[If no, then skip to question 4.]</td>
</tr>
<tr>
<td>3</td>
<td>Before the patient started testosterone therapy, did the patient have a confirmed low testosterone level according to current practice guidelines or your standard lab reference values?</td>
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<tr>
<td></td>
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</tr>
<tr>
<td></td>
<td>[No further questions.]</td>
</tr>
<tr>
<td>4</td>
<td>Does the patient have at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values?</td>
</tr>
<tr>
<td></td>
<td>Yes No</td>
</tr>
<tr>
<td></td>
<td>[No further questions.]</td>
</tr>
<tr>
<td>5</td>
<td>Is the requested drug being prescribed for inoperable metastatic breast cancer in a patient who is 1 to 5 years postmenopausal?</td>
</tr>
<tr>
<td></td>
<td>Yes No</td>
</tr>
<tr>
<td></td>
<td>[If yes, then no further questions.]</td>
</tr>
<tr>
<td>6</td>
<td>Is the requested drug being prescribed for a premenopausal patient with breast cancer who has benefited from oophorectomy and is considered to have a hormone-responsive tumor?</td>
</tr>
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7. Is the requested drug being prescribed for delayed puberty? Yes  No

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<tr>
<td>2. Go to 3</td>
<td>Go to 4</td>
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</table>
| 3. Approve, 36 Months | Deny | You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions:  
- You have primary or hypogonadotropic hypogonadism  
- Before starting testosterone therapy, you had a test that showed low testosterone levels  
Your request has been denied based on the information we have.  
[Short Description: No confirmation of diagnosis (tests, labs, etc.]] |
| 4. Approve, 36 Months | Deny | You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions:  
- You have primary or hypogonadotropic hypogonadism  
- You have had 2 tests that showed low testosterone levels  
Your request has been denied based on the information we have.  
[Short Description: No confirmation of diagnosis (tests, labs, etc.]] |
| 5. Approve, 36 months | Go to 6 |
| 6. Approve, 36 months | Go to 7 |
| 7. Approve, 36 Months | Deny | You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions:  
- You have primary or hypogonadotropic hypogonadism  
- You are postmenopausal with metastatic breast cancer and surgery is not possible  
- You are premenopausal with breast cancer, have a hormone-responsive tumor, and had your ovaries removed  
- You have delayed puberty  
Your request has been denied based on the information we have.  
[Short Description: No approvable diagnosis] |
PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>TESTOSTERONE PRODUCTS – INJECTABLE</th>
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</thead>
<tbody>
<tr>
<td>BRAND NAME*</td>
<td>DELATESTRYL (testosterone enanthate injection)</td>
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<td>(generic)</td>
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**Status:** CVS Caremark Criteria  
**Type:** Initial Prior Authorization  
**MDC-2 Ref #** 906-A

*Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

**FDA-APPROVED INDICATIONS**

**Delatestryl**

**Males**

Delatestryl (Testosterone Enanthate Injection) is indicated for replacement therapy in conditions associated with a deficiency or absence of endogenous testosterone.

- **Primary hypogonadism** (congenital or acquired) - testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, or orchiectomy.
- **Hypogonadotropic hypogonadism** (congenital or acquired) - gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation. (Appropriate adrenal cortical and thyroid hormone replacement therapy are still necessary, however, and are actually of primary importance).

If the above conditions occur prior to puberty, androgen replacement therapy will be needed during the adolescent years for development of secondary sexual characteristics. Prolonged androgen treatment will be required to maintain sexual characteristics in these and other males who develop testosterone deficiency after puberty.

Safety and efficacy of Delatestryl in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.

- **Delayed puberty** - Delatestryl (Testosterone Enanthate Injection) may be used to stimulate puberty in carefully selected males with clearly delayed puberty. These patients usually have a familial pattern of delayed puberty that is not secondary to a pathological disorder; puberty is expected to occur spontaneously at a relatively late date. Brief treatment with conservative doses may occasionally be justified in these patients if they do not respond to psychological support. The potential adverse effect on bone maturation should be discussed with the patient and parents prior to androgen administration. An X-ray of the hand and wrist to determine bone age should be obtained every six months to assess the effect of treatment on the epiphyseal centers.

**Females**

Metastatic Mammary Cancer - Delatestryl (Testosterone Enanthate Injection) may be used secondarily in women with advancing inoperable metastatic (skeletal) mammary cancer who are one to five years postmenopausal. Primary goals of therapy in these women include ablation of the ovaries. Other methods of countereacting estrogen activity are adrenalectomy, hypophysectomy, and/or anti-estrogen therapy. This treatment has also been used in pre-menopausal women with breast cancer who have benefited from oophorectomy and are considered to have a hormone-responsive tumor. Judgment concerning androgen therapy should be made by an oncologist with expertise in this field.

**Xyosted**

Xyosted (testosterone enanthate) injection is an androgen indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone:
- Primary hypogonadism (congenital or acquired): testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchietomy, Klinefelter’s syndrome, chemotherapy, or toxic damage from alcohol or heavy meals. These men usually have low serum testosterone concentrations and gonadotropins (follicle-stimulating hormone [FSH], luteinizing hormone [LH]) above the normal range.
- Hypogonadotropic hypogonadism (congenital or acquired): gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations but have gonadotropins in the low or normal range.

Limitations of Use
- Safety and efficacy of Xyosted in adult males with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.
- Safety and efficacy of Xyosted in males less than 18 years of age have not been established.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:
- The requested drug is being prescribed for primary or hypogonadotropic hypogonadism [Note: Safety and efficacy of testosterone products in patients with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.]
  AND
    o Before the start of testosterone therapy, the patient has at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values OR
    o For continuation of testosterone therapy: before the patient started testosterone therapy, the patient had a confirmed low testosterone level according to current practice guidelines or your standard lab reference values OR
- Testosterone enanthate injection (generic Delatestryl) is being prescribed for inoperable metastatic breast cancer in a patient who is 1 to 5 years postmenopausal AND the patient had an incomplete response to other therapy for metastatic breast cancer OR
- Testosterone enanthate injection (generic Delatestryl) is being prescribed for a premenopausal patient with breast cancer who has benefited from oophorectomy and is considered to have a hormone-responsive tumor OR
- Testosterone enanthate injection (generic Delatestryl) is being prescribed for delayed puberty

RATIONALE
These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. In males, Delatestryl and Xyosted are indicated for replacement therapy in conditions associated with a deficiency or absence of endogenous testosterone: primary hypogonadism (testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, or orchietomy) or hypogonadotropic hypogonadism (gonadotropin or luteinizing hormone-releasing hormone [LHRH] deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation). Delatestryl is also indicated for delayed puberty. Safety and efficacy of Delatestryl and Xyosted in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.1-4

A testosterone determination, in conjunction with a free testosterone or sex hormone-binding globulin level, is the threshold test in the evaluation of suspected male hypogonadism (serum total testosterone levels less than 300 ng/dL). Testosterone levels should be determined in the morning, and studies should be repeated in patients with subnormal levels. The normative ranges for total and free testosterone levels in healthy young men vary among laboratories and assays. In some laboratories, the lower limit of the normal range for total testosterone level in healthy young men is 280-
300 ng/dL and for serum free testosterone level is 5–9 pg/mL. The clinicians should use the lower limit of normal range for healthy young men established in their laboratory.5,6 For initial therapy, testosterone will be approved for patients with at least two confirmed low testosterone levels according to current practice guidelines or standard lab reference values. If the patient is already on testosterone therapy and did not get a repeat testosterone level before starting therapy, it would be inappropriate for the patient to stop treatment to get a repeat testosterone level. For continuation of therapy, one low testosterone level is required before the patient started testosterone therapy.

Delatestryl may be used secondarily in women with advancing inoperable metastatic (skeletal) mammary cancer who are one to five years postmenopausal. Primary goals of therapy in these women include ablation of the ovaries. Other methods of countering estrogen activity are adrenalectomy, hypophysectomy, and/or anti-estrogen therapy.1, 3-4 Since testosterone is not a first-line drug for breast cancer, the patient must have had an incomplete response to other breast cancer therapy before using testosterone.

This treatment has also been used in premenopausal women with breast cancer who have benefited from oophorectomy and are considered to have a hormone-responsive tumor. Judgment concerning androgen therapy should be made by an oncologist with expertise in this field.1, 3-4

Delatestryl may be used to stimulate puberty in carefully selected males with clearly delayed puberty. Brief treatment with conservative doses may occasionally be justified in these patients if they do not respond to psychological support.1, 3-4

REFERENCES
2. Is this request for a continuation of testosterone therapy? [Yes] [No] [If no, then skip to question 4.]

3. Before the patient started testosterone therapy, did the patient have a confirmed low testosterone level according to current practice guidelines or your standard lab reference values? [Yes] [No] [No further questions.]

4. Does the patient have at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values? [Yes] [No] [No further questions.]

5. Is testosterone enanthate injection (generic Delatestryl) being prescribed for inoperable metastatic breast cancer in a patient who is 1 to 5 years postmenopausal AND has the patient had an incomplete response to other therapy for metastatic breast cancer? [Yes] [No] [If yes, then no further questions.]

6. Is testosterone enanthate injection (generic Delatestryl) being prescribed for a premenopausal patient with breast cancer who has benefited from oophorectomy and is considered to have a hormone-responsive tumor? [Yes] [No] [If yes, then no further questions.]

7. Is testosterone enanthate injection (generic Delatestryl) being prescribed for delayed puberty? [Yes] [No]

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**Guidelines for Approval**

<table>
<thead>
<tr>
<th>Set 1</th>
<th>Set 2</th>
<th>Set 3</th>
</tr>
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<tbody>
<tr>
<td><strong>Duration of Approval</strong></td>
<td>12 Months</td>
<td></td>
</tr>
<tr>
<td><strong>Yes to question(s)</strong></td>
<td><strong>No to question(s)</strong></td>
<td><strong>Yes to question(s)</strong></td>
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<td></td>
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<td><strong>Set 4</strong></td>
<td><strong>Set 5</strong></td>
<td></td>
</tr>
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<td><strong>No to question(s)</strong></td>
<td><strong>Yes to question(s)</strong></td>
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**Mapping Instructions**

<table>
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<th>No</th>
</tr>
</thead>
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<td>1. Go to 2</td>
<td>Go to 5</td>
</tr>
<tr>
<td>2. Go to 3</td>
<td>Go to 4</td>
</tr>
<tr>
<td>3. Approve, 12 Months</td>
<td>Deny</td>
</tr>
<tr>
<td>4. Approve, 12 Months</td>
<td>Deny</td>
</tr>
</tbody>
</table>

**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**

3. Approve, 12 Months

You do not meet the requirements of your plan. Your plan covers this drug when you have had a test that showed low testosterone levels before you started testosterone therapy. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (tests, labs, etc.)]

4. Approve, 12 Months

You do not meet the requirements of your plan. Your plan covers this drug when you have had two tests that showed low testosterone levels. Your request has been denied based on the information we have.
<table>
<thead>
<tr>
<th>5. Approve, 12 Months</th>
<th>Go to 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>6. Approve, 12 Months</td>
<td>Go to 7</td>
</tr>
<tr>
<td>7. Approve, 12 Months</td>
<td>Deny</td>
</tr>
</tbody>
</table>

You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions:
- You have primary or hypogonadotropic hypogonadism
- For testosterone enanthate injection (generic Delatestryl), you are a postmenopausal patient with metastatic breast cancer, surgery is not possible, and other drugs for your cancer did not work for you
- For testosterone enanthate injection (generic Delatestryl), you are a premenopausal patient with breast cancer, have a hormone-responsive tumor, and had your ovaries removed
- Testosterone enanthate injection (generic Delatestryl) is being prescribed for delayed puberty

Your request has been denied based on the information we have.

[Short Description: No approvable diagnosis]
## PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>TESTOSTERONE PRODUCTS – INJECTABLE</th>
</tr>
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<tbody>
<tr>
<td>BRAND NAME* (generic)</td>
<td>DELATESTRYL (testosterone enanthate injection)</td>
</tr>
<tr>
<td></td>
<td>XYOSTED (testosterone enanthate injection)</td>
</tr>
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</table>

**Status:** CVS Caremark Criteria  
**Type:** Initial Prior Authorization  
**Ref # 1368-A**

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

### FDA-APPROVED INDICATIONS

**Delatestryl**

**Males**

Delatestryl (Testosterone Enanthate Injection) is indicated for replacement therapy in conditions associated with a deficiency or absence of endogenous testosterone.

- **Primary hypogonadism** (congenital or acquired) - testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, or orchiectomy.
- **Hypogonadotropic hypogonadism** (congenital or acquired) - gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation. (Appropriate adrenal cortical and thyroid hormone replacement therapy are still necessary, however, and are actually of primary importance).  

If the above conditions occur prior to puberty, androgen replacement therapy will be needed during the adolescent years for development of secondary sexual characteristics. Prolonged androgen treatment will be required to maintain sexual characteristics in these and other males who develop testosterone deficiency after puberty. Safety and efficacy of Delatestryl in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.

- **Delayed puberty** - Delatestryl (Testosterone Enanthate Injection) may be used to stimulate puberty in carefully selected males with clearly delayed puberty. These patients usually have a familial pattern of delayed puberty that is not secondary to a pathological disorder; puberty is expected to occur spontaneously at a relatively late date. Brief treatment with conservative doses may occasionally be justified in these patients if they do not respond to psychological support. The potential adverse effect on bone maturation should be discussed with the patient and parents prior to androgen administration. An X-ray of the hand and wrist to determine bone age should be obtained every six months to assess the effect of treatment on the epiphyseal centers.

**Females**

- **Metastatic Mammary Cancer** - Delatestryl (Testosterone Enanthate Injection) may be used secondarily in women with advancing inoperable metastatic (skeletal) mammary cancer who are one to five years postmenopausal. Primary goals of therapy in these women include ablation of the ovaries. Other methods of countereacting estrogen activity are adrenalecetomy, hypophysectomy, and/or anti-estrogen therapy. This treatment has also been used in pre-menopausal women with breast cancer who have benefited from oophorectomy and are considered to have a hormone-responsive tumor. Judgment concerning androgen therapy should be made by an oncologist with expertise in this field.

**Xyosted**

Xyosted (testosterone enanthate) injection is an androgen indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone:
- Primary hypogonadism (congenital or acquired): testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchietomy, Klinefelter’s syndrome, chemotherapy, or toxic damage from alcohol or heavy meals. These men usually have low serum testosterone concentrations and gonadotropins (follicle-stimulating hormone [FSH], luteinizing hormone [LH]) above the normal range.
- Hypogonadotropic hypogonadism (congenital or acquired): gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations but have gonadotropins in the low or normal range.

Limitations of Use
- Safety and efficacy of Xyosted in adult males with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.
- Safety and efficacy of Xyosted in males less than 18 years of age have not been established.

Compendial Uses
Gender Dysphoria in transgender male patients\textsuperscript{4,7-10}

**COVERAGE CRITERIA**
The requested drug will be covered with prior authorization when the following criteria are met:
- The requested drug is being prescribed for primary or hypogonadotropic hypogonadism [Note: Safety and efficacy of testosterone products in patients with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.]
  - Before the start of testosterone therapy, the patient has at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values
  - For continuation of testosterone therapy: before the patient started testosterone therapy, the patient had a confirmed low testosterone level according to current practice guidelines or your standard lab reference values
- The requested drug is being prescribed for gender dysphoria in a patient who is able to make an informed decision to engage in hormone therapy
- Testosterone enanthate injection (generic Delatestryl) is being prescribed for delayed puberty
- Testosterone enanthate injection (generic Delatestryl) is being prescribed for inoperable metastatic breast cancer in a patient who is 1 to 5 years postmenopausal AND the patient had an incomplete response to other therapy for metastatic breast cancer
- Testosterone enanthate injection (generic Delatestryl) is being prescribed for a pre-menopausal patient with breast cancer who has benefited from oophorectomy and is considered to have a hormone-responsive tumor

**RATIONALE**
The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. In males, Delatestryl is indicated for replacement therapy in conditions associated with a deficiency or absence of endogenous testosterone: primary hypogonadism (testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, or orchietomy) or hypogonadotropic hypogonadism (gonadotropin or luteinizing hormone-releasing hormone [LHRH] deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation). Delatestryl is also indicated for delayed puberty. Safety and efficacy of Delatestryl and Xyosted in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.\textsuperscript{1-4}

A testosterone determination, in conjunction with a free testosterone or sex hormone-binding globulin level, is the threshold test in the evaluation of suspected male hypogonadism (serum total testosterone levels less than 300 ng/dL [nanograms per deciliter]). Testosterone levels should be determined in the morning, and studies should be repeated in
patients with subnormal levels. The normative ranges for total and free testosterone levels in healthy young men vary among laboratories and assays. In some laboratories, the lower limit of the normal range for total testosterone level in healthy young men is 280-300 ng/dL and for serum free testosterone level is 5–9 pg/mL (picograms per milliliter). Clinicians should use the lower limit of normal range for healthy young men established in their laboratory. For initial therapy, testosterone will be approved for patients with at least two confirmed low testosterone levels according to current practice guidelines or standard lab reference values. If the patient is already on testosterone therapy and did not get a repeat testosterone level before starting therapy, it would be inappropriate for the patient to stop treatment to get a repeat testosterone level. For continuation of therapy, one low testosterone level is required before the patient started testosterone therapy.

Delatestryl may be used secondarily in women with advancing inoperable metastatic (skeletal) mammary cancer who are one to five years postmenopausal. Primary goals of therapy in these women include ablation of the ovaries. Other methods of counteracting estrogen activity are adrenalectomy, hypophysectomy, and/or anti-estrogen therapy. Since testosterone is not a first-line drug for breast cancer, the patient must have had an incomplete response to other breast cancer therapy before using testosterone.

This treatment has also been used in pre-menopausal women with breast cancer who have benefited from oophorectomy and are considered to have a hormone-responsive tumor. Judgment concerning androgen therapy should be made by an oncologist with expertise in this field.

Delatestryl may be used to stimulate puberty in carefully selected males with clearly delayed puberty. Brief treatment with conservative doses may occasionally be justified in these patients if they do not respond to psychological support.

Testosterone enanthate injection has a compendial use for gender dysphoria in transgender male (female-to-male) patients.

Transgender persons seeking to develop the physical characteristics of the desired gender require a safe, effective hormone regimen that will suppress endogenous hormone secretion determined by the person’s genetic/biologic sex and maintain sex hormone levels within the normal range for the person’s desired gender. The two major goals of hormonal therapy are to reduce endogenous hormone levels and, thereby, the secondary sex characteristics of the individual’s biological/genetic sex and to replace endogenous sex hormone levels with those of the reassigned sex. The Endocrine Society suggests that pubertal development of the desired opposite sex be initiated at about the age of 16 years, using a gradually increasing dose schedule of cross-sex steroids. However, the Endocrine Society Guidelines also state that identifying an age at which pubertal development is initiated can be difficult and may depend on several factors (such as the age when pubertal suppression was begun, medications used to initiate pubertal suppression, and relative risks of prolonged pubertal suppression), and the goal is to start the process at a time when the individual will be able to make informed, mature decisions to engage in the therapy. Some patients may advance to Tanner stage 2 of pubertal development at an early age (such as 9 or 10) and using pubertal suppression therapy for 6 or 7 years may be deemed inappropriate. Medical professionals involved in the patient’s care should be involved in assessing whether the patient is ready to make the decision to begin hormone therapy and pubertal development. Therefore, individuals who are able to make an informed decision to engage in hormone therapy will be approved.

For transgender male persons, regimens to change secondary sex characteristics follow the general principle of hormone replacement treatment of male hypogonadism. Either parenteral or transdermal preparations can be used to achieve testosterone values in the normal male range (320-1000 ng/dL). The agent primarily used for endocrine treatment of transgender male patients is testosterone. When determining the appropriate method of testosterone delivery, many considerations should be taken into account. The most well-described formulation of testosterone therapy used to treat transgender male patients is intramuscular injection of testosterone esters (cypionate or enanthate). Because intramuscular testosterone cypionate or enanthate is often administered every 2-4 weeks, some patients may notice a cyclic variation in effects as well as more time outside the normal physiologic levels. Due to this cyclic variation, other preparations such as weekly subcutaneous testosterone enanthate injection may be considered.

REFERENCES

**CRITERIA FOR APPROVAL**

1. Is the requested drug being prescribed for primary or hypogonadotropic hypogonadism?  
   [Note: Safety and efficacy of testosterone products in patients with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.]  
   [If no, then skip to question 5.]
   Yes  No

2. Is this request for a continuation of testosterone therapy?  
   [If no, then skip to question 4.]
   Yes  No

3. Before the patient started testosterone therapy, did the patient have a confirmed low testosterone level according to current practice guidelines or your standard lab reference values?  
   [No further questions.]
   Yes  No

4. Does the patient have at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values?  
   [No further questions.]
   Yes  No

5. Is the requested drug being prescribed for gender dysphoria in a patient who is able to make an informed decision to engage in hormone therapy?  
   [If yes, then no further questions.]
   Yes  No
<table>
<thead>
<tr>
<th></th>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>Is testosterone enanthate injection (generic Delatestryl) being prescribed for delayed puberty?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>[If yes, then no further questions.]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Is testosterone enanthate injection (generic Delatestryl) being prescribed for inoperable metastatic breast cancer in a patient who is 1 to 5 years postmenopausal AND has the patient had an incomplete response to other therapy for metastatic breast cancer?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>[If yes, then no further questions.]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Is testosterone enanthate injection (generic Delatestryl) being prescribed for a premenopausal patient with breast cancer who has benefited from oophorectomy and is considered to have a hormone-responsive tumor?</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

**Mapping Instructions**

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
<th>DENIAL REASONS – DO NOT USE FOR MEDICARE PART D</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Go to 2</td>
<td>Go to 5</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have had a test that showed low testosterone levels before you started testosterone therapy. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (tests, labs, etc.)]</td>
</tr>
<tr>
<td>2. Go to 3</td>
<td>Go to 4</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have had two tests that showed low testosterone levels. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (tests, labs, etc.)]</td>
</tr>
<tr>
<td>3. Approve, 12 months</td>
<td>Deny</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have had a test that showed low testosterone levels before you started testosterone therapy. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (tests, labs, etc.)]</td>
</tr>
<tr>
<td>4. Approve, 12 months</td>
<td>Deny</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have had two tests that showed low testosterone levels. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (tests, labs, etc.)]</td>
</tr>
<tr>
<td>5. Approve, 12 months</td>
<td>Go to 6</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have had a test that showed low testosterone levels before you started testosterone therapy. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (tests, labs, etc.)]</td>
</tr>
<tr>
<td>6. Approve, 12 months</td>
<td>Go to 7</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have had a test that showed low testosterone levels before you started testosterone therapy. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (tests, labs, etc.)]</td>
</tr>
<tr>
<td>7. Approve, 12 months</td>
<td>Go to 8</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have had a test that showed low testosterone levels before you started testosterone therapy. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (tests, labs, etc.)]</td>
</tr>
<tr>
<td>8. Approve, 12 months</td>
<td>Deny</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions: - You have primary or hypogonadotrophic hypogonadism - You have gender dysphoria and you can make an informed decision to use this drug - Testosterone enanthate injection (generic Delatestryl) is being prescribed for delayed puberty - For testosterone enanthate injection (generic Delatestryl), you are a postmenopausal patient with metastatic breast cancer, surgery is not possible, and other drugs for your cancer did not work for you - For testosterone enanthate injection (generic Delatestryl), you are a premenopausal patient with breast cancer, have a hormone-responsive tumor, and had your ovaries removed Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]</td>
</tr>
</tbody>
</table>

Testosterone - Testosterone Enanthate TGC 1368-A 02-2019

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# PRIOR AUTHORIZATION CRITERIA

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<tr>
<th>DRUG CLASS</th>
<th>TESTOSTERONE PRODUCTS – TOPICAL/BUCCAL/NASAL</th>
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<tbody>
<tr>
<td>BRAND NAME*</td>
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<tbody>
<tr>
<td>Type:</td>
<td>Initial Prior Authorization</td>
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</table>

*Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

## FDA-APPROVED INDICATIONS

Topical, buccal, and nasal testosterone products are indicated for replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone.

**Primary hypogonadism** (congenital or acquired) - testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter Syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations and gonadotropins (FSH, LH) above the normal range.

**Hypogonadotropic hypogonadism** (congenital or acquired) - gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations but have gonadotropins in the normal or low range.

## Limitations of Use

Testosterone - Topical, Buccal, Nasal Non-TGC MDC-2 229-A 10-2018  
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Safety and efficacy of topical, buccal, and nasal testosterone products in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.

Safety and efficacy of topical, buccal, and nasal testosterone products in males less than 18 years old have not been established.

Topical testosterone products may have different doses, strengths or application instructions that may result in different systemic exposure.

**COVERAGE CRITERIA**
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for primary or hypogonadotropic hypogonadism [Note: Safety and efficacy of testosterone products in patients with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.]

  **AND**
  - Before the start of testosterone therapy, the patient has at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values **OR**
  - For continuation of testosterone therapy: before the patient started testosterone therapy, the patient had a confirmed low testosterone level according to current practice guidelines or your standard lab reference values

**RATIONALE**
These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Topical, buccal, and nasal testosterone products are indicated for replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone: congenital or acquired primary hypogonadism (testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter Syndrome, chemotherapy, or toxic damage from alcohol or heavy metals), congenital or acquired hypogonadotropic hypogonadism (gonadotropin or luteinizing hormone-releasing hormone [LHRH] deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation). Safety and efficacy of topical, buccal, and nasal testosterone products in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.1-11

A testosterone determination, in conjunction with a free testosterone or sex hormone-binding globulin level, is the threshold test in the evaluation of suspected male hypogonadism (serum total testosterone levels less than 300 ng/dL). Testosterone levels should be determined in the morning, and studies should be repeated in patients with subnormal levels. The normative ranges for total and free testosterone levels in healthy young men vary among laboratories and assays. In some laboratories, the lower limit of the normal range for total testosterone level in healthy young men is 280-300 ng/dL and for serum free testosterone level is 5–9 pg/mL. The clinicians should use the lower limit of normal range for healthy young men established in their laboratory.12,13 For initial therapy, testosterone will be approved for patients with at least two confirmed low testosterone levels according to current practice guidelines or standard lab reference values. If the patient is already on testosterone therapy and did not get a repeat testosterone level before starting therapy, it would be inappropriate for the patient to stop treatment to get a repeat testosterone level. For continuation of therapy, one low testosterone level is required before the patient started testosterone therapy.

**REFERENCES**

Written by: UM Development (AH) Date: 07/2003
Revised: (NB) 01/2005, (MG) 02/2006; (NB) 02/2007(2); (AM) 01/2008, 12/2008; (MS) 11/2009, 12/2010, (TM) 11/2011; (PL) 10/2012 (created MDC-2 due to extended commercial duration), 11/2012; (CS) 08/2013; (PL) 11/2013, (SE) 04/2014 (rephrased diagnosis question); (RP) 06/2014 (Add Natesto), (PL) 06/2014 (Add Vogelxo); (CF/JH) 11/2014, 02/2015 (updated testosterone level question), (LN) 04/2015 (added denial reasons); (CF/JH) 11/2015, (SE) 06/2016 (created separate Med D); (CF/JH) 11/2016; (KC) 11/2017, 10/2018 (no clinical changes), 08/2019 (removed “male” from lab questions)

CRITERIA FOR APPROVAL

| 1 | Is the requested drug being prescribed for primary or hypogonadotrophic hypogonadism? | Yes | No |

[Note: Safety and efficacy of testosterone products in patients with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.]

| 2 | Is this request for a continuation of testosterone therapy? | Yes | No |

[If no, then skip to question 4.]

| 3 | Before the patient started testosterone therapy, did the patient have a confirmed low testosterone level according to current practice guidelines or your standard lab reference values? | Yes | No |

[No further questions.]

| 4 | Does the patient have at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values? | Yes | No |

Guidelines for Approval

<table>
<thead>
<tr>
<th>Duration of Approval</th>
<th>12 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes to question(s)</td>
<td>No to question(s)</td>
</tr>
<tr>
<td>1</td>
<td>None</td>
</tr>
<tr>
<td>4</td>
<td></td>
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Testosterone - Topical, Buccal, Nasal Non-TGC MDC-2 229-A 10-2018 ©2019 CVS Caremark. All rights reserved.

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## Mapping Instructions

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
<th>DENIAL REASONS – DO NOT USE FOR MEDICARE PART D</th>
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</thead>
<tbody>
<tr>
<td>1. Go to 2</td>
<td>Deny</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have primary or hypogonadotropic hypogonadism. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]</td>
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<tr>
<td>2. Go to 3</td>
<td>Go to 4</td>
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<td></td>
</tr>
<tr>
<td>3. Approve, 12 months</td>
<td>Deny</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have had a test that showed low testosterone levels before you started testosterone therapy. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (tests, labs, etc.)]</td>
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<tr>
<td>4. Approve, 12 months</td>
<td>Deny</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have had two tests that showed low testosterone levels. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (tests, labs, etc.)]</td>
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## PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>TESTOSTERONE PRODUCTS – TOPICAL/BUCCAL/NASAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRAND NAME*</td>
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<tr>
<td>(generic)</td>
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</tr>
<tr>
<td>ANDRODERM</td>
<td></td>
</tr>
<tr>
<td>(testosterone transdermal patch)</td>
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<tr>
<td>ANDROGEL</td>
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<tr>
<td>(testosterone topical gel)</td>
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</tr>
<tr>
<td>AXIRON</td>
<td></td>
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<tr>
<td>(testosterone topical solution)</td>
<td></td>
</tr>
<tr>
<td>FORTESTA</td>
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<tr>
<td>(testosterone topical gel)</td>
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<tr>
<td>NATESTO</td>
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<tr>
<td>(testosterone nasal gel)</td>
<td></td>
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<tr>
<td>STRIANT</td>
<td></td>
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<tr>
<td>(testosterone mucoadhesive buccal system)</td>
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<tr>
<td>TESTIM</td>
<td></td>
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<tr>
<td>(testosterone topical gel)</td>
<td></td>
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<tr>
<td>VOGELXO</td>
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<tr>
<td>(testosterone topical gel)</td>
<td></td>
</tr>
</tbody>
</table>

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

**FDA-APPROVED INDICATIONS**

Topical, buccal, and nasal testosterone products are indicated for replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone.

Primary hypogonadism (congenital or acquired) - testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchectomy, Klinefelter Syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations and gonadotropins (FSH, LH) above the normal range.

Hypogonadotropic hypogonadism (congenital or acquired) - gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations but have gonadotropins in the normal or low range.

**Limitations of Use**
Safety and efficacy of topical, buccal, and nasal testosterone products in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.

Safety and efficacy of topical, buccal, and nasal testosterone products in males less than 18 years old have not been established.

Topical testosterone products may have different doses, strengths or application instructions that may result in different systemic exposure.

Compendial Uses
Gender Dysphoria in transgender male patients

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for primary or hypogonadotropic hypogonadism [Note: Safety and efficacy of testosterone products in patients with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.]
  AND
  o Before the start of testosterone therapy, the patient has at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values OR
  o For continuation of testosterone therapy: before the patient started testosterone therapy, the patient had a confirmed low testosterone level according to current practice guidelines or your standard lab reference values

OR
- The requested drug is being prescribed for gender dysphoria in a patient who is able to make an informed decision to engage in hormone therapy

RATIONALE
The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Topical, buccal, and nasal testosterone products are indicated for replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone: congenital or acquired primary hypogonadism (testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter Syndrome, chemotherapy, or toxic damage from alcohol or heavy metals), congenital or acquired hypogonadotropic hypogonadism (gonadotropin or luteinizing hormone-releasing hormone [LHRH] deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation). Safety and efficacy of topical, buccal, and nasal testosterone products in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.

A testosterone determination, in conjunction with a free testosterone or sex hormone-binding globulin level, is the threshold test in the evaluation of suspected male hypogonadism (serum total testosterone levels less than 300 ng/dL [nanograms per deciliter]). Testosterone levels should be determined in the morning, and studies should be repeated in patients with subnormal levels. The normative ranges for total and free testosterone levels in healthy young men vary among laboratories and assays. In some laboratories, the lower limit of the normal range for total testosterone level in healthy young men is 280-300 ng/dL and for serum free testosterone level is 5–9 pg/mL (picograms per milliliter). Clinicians should use the lower limit of normal range for healthy young men established in their laboratory. For initial therapy, testosterone will be approved for patients with at least two confirmed low testosterone levels according to current practice guidelines or standard lab reference values. If the patient is already on testosterone therapy and did not get a repeat testosterone level before starting therapy, it would be inappropriate for the patient to stop treatment to get a repeat testosterone level. For continuation of therapy, one low testosterone level is required before the patient started testosterone therapy.

Topical, buccal, and nasal testosterone products have a compendial use for gender dysphoria in transgender male (female-to-male) patients.
Transgender persons seeking to develop the physical characteristics of the desired gender require a safe, effective hormone regimen that will suppress endogenous hormone secretion determined by the person’s genetic/biologic sex and maintain sex hormone levels within the normal range for the person’s desired gender. The two major goals of hormonal therapy are to reduce endogenous hormone levels and, thereby, the secondary sex characteristics of the individual’s biological/genetic sex and to replace endogenous sex hormone levels with those of the reassigned sex. The Endocrine Society suggests that pubertal development of the desired opposite sex be initiated at about the age of 16 years, using a gradually increasing dose schedule of cross-sex steroids. However, the Endocrine Society Guidelines also state that identifying an age at which pubertal development is initiated can be difficult and may depend on several factors (such as the age when pubertal suppression was begun, medications used to initiate pubertal suppression, and relative risks of prolonged pubertal suppression), and the goal is to start the process at a time when the individual will be able to make informed, mature decisions to engage in the therapy. Some patients may advance to Tanner stage 2 of pubertal development at an early age (such as 9 or 10) and using pubertal suppression therapy for 6 or 7 years may be deemed inappropriate. Medical professionals involved in the patient’s care should be involved in assessing whether the patient is ready to make the decision to begin hormone therapy and pubertal development. Therefore, individuals who are able to make an informed decision to engage in hormone therapy will be approved.

For transgender male (female-to-male) persons, regimens to change secondary sex characteristics follow the general principle of hormone replacement treatment of male hypogonadism. Either parenteral or transdermal preparations can be used to achieve testosterone values in the normal male range (320-1000 ng/dL). The agent primarily used for endocrine treatment of transgender male patients is testosterone. When determining the appropriate method of testosterone delivery, many considerations should be taken into account. The most well-described formulation of testosterone therapy used to treat transgender male patients is intramuscular injection of testosterone esters (cypionate or enanthate). Because intramuscular testosterone cypionate or enanthate is often administered every 2-4 weeks, some patients may notice a cyclic variation in effects as well as more time outside the normal physiologic levels. Transdermal testosterone has been shown to provide less variation in serum testosterone levels compared with injectable preparations. Testosterone administered transdermally more closely mimics physiologic testosterone levels. However, transdermal preparations achieve low-normal ranges of testosterone levels in hypogonadal men, which may translate to a lessened change in physical appearance and virilization in the transgender male patient.

REFERENCES

Testosterone - Topical, Buccal, Nasal TGC 1370-A 02-2019 ©2019 CVS Caremark. All rights reserved.
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CRITERIA FOR APPROVAL

1. Is the requested drug being prescribed for primary or hypogonadotropic hypogonadism?  
   [Note: Safety and efficacy of testosterone products in patients with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.]  
   [If no, then skip to question 5.]  
   Yes  
   No

2. Is this request for a continuation of testosterone therapy?  
   [If no, then skip to question 4.]  
   Yes  
   No

3. Before the patient started testosterone therapy, did the patient have a confirmed low testosterone level according to current practice guidelines or your standard lab reference values?  
   [No further questions.]  
   Yes  
   No

4. Does the patient have at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values?  
   [No further questions.]  
   Yes  
   No

5. Is the requested drug being prescribed for gender dysphoria in a patient who is able to make an informed decision to engage in hormone therapy?  
   Yes  
   No

Mapping Instructions

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
<th>DENIAL REASONS – DO NOT USE FOR MEDICARE PART D</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Go to 2</td>
<td>Go to 5</td>
</tr>
<tr>
<td>2.</td>
<td>Go to 3</td>
<td>Go to 4</td>
</tr>
<tr>
<td>3.</td>
<td>Approve, 12 months</td>
<td>Deny</td>
</tr>
<tr>
<td>4.</td>
<td>Approve, 12 months</td>
<td>Deny</td>
</tr>
<tr>
<td>5.</td>
<td>Approve, 12 months</td>
<td>Deny</td>
</tr>
</tbody>
</table>

You do not meet the requirements of your plan. Your plan covers this drug when you have had a test that showed low testosterone levels before you started testosterone therapy. Your request has been denied based on the information we have.  
[Short Description: no confirmation of diagnosis (tests, labs, etc.)]
Your request has been denied based on the information we have.
[Short Description: no approvable diagnosis]
POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
   Treatment of chorea associated with Huntington’s disease

B. Compendial Uses
   1. Chronic tics
   2. Tardive dyskinesia
   3. Hemiballismus
   4. Chorea not associated with Huntington’s disease

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR APPROVAL

A. Chorea
   Authorization of 12 months may be granted for treatment of chorea.

B. Chronic tics
   Authorization of 12 months may be granted for treatment of chronic tics.

C. Tardive dyskinesia
   Authorization of 12 months may be granted for the treatment of tardive dyskinesia.

D. Hemiballismus
   Authorization of 12 months may be granted for the treatment of hemiballismus.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

2. Micromedex® (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. Available at:
SPECIALTY GUIDELINE MANAGEMENT

THALOMID (thalidomide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Thalomid in combination with dexamethasone is indicated for the treatment of patients with newly diagnosed multiple myeloma.
   2. Erythema Nodosum Leprosum (ENL)
      a. Acute treatment of the cutaneous manifestations of moderate to severe ENL
      b. Maintenance therapy for prevention and suppression of the cutaneous manifestations of ENL recurrence
      Limitations of Use: not indicated as monotherapy for ENL treatment in the presence of moderate to severe neuritis

B. Compendial Uses
   1. Myelofibrosis-related anemia
   2. Multicentric Castleman’s disease
   3. Recurrent aphthous stomatitis
   4. Recurrent HIV-associated aphthous ulcers
   5. Cachexia in patients with cancer or HIV-associated wasting syndrome
   6. Diarrhea in patients with HIV infection
   7. Kaposi’s sarcoma in HIV-infected patients
   8. Behçet’s syndrome
   9. Chronic graft-versus-host disease
   10. Crohn’s disease

All other indications are considered experimental/investigational and are not covered benefits.

II. CRITERIA FOR INITIAL APPROVAL

A. Multiple Myeloma
   Authorization of 12 months may be granted for treatment of multiple myeloma.

B. Recurrent HIV-associated Aphthous Ulcers
   Authorization of 12 months may be granted for treatment of recurrent HIV-associated aphthous ulcers.

C. Behçet’s Syndrome
   Authorization of 12 months may be granted for treatment of Behçet’s syndrome.

D. Myelofibrosis-related Anemia
   Authorization of 12 months may be granted for treatment of myelofibrosis-related anemia.

E. Erythema Nodosum Leprosum
Authorization of 12 months may be granted for treatment of erythema nodosum leprosum.

F. Crohn’s Disease
Authorization of 12 months may be granted for treatment of Crohn’s disease.

G. Kaposi’s Sarcoma
Authorization of 12 months may be granted for treatment of Kaposi’s sarcoma in HIV-infected patients.

H. Chronic Graft-versus-Host Disease
Authorization of 12 months may be granted for treatment of chronic graft-versus-host disease.

I. Multicentric Castleman’s Disease
Authorization of 12 months may be granted for treatment of multicentric Castleman’s disease.

J. Recurrent Aphthous Stomatitis
Authorization of 12 months may be granted for treatment of recurrent aphthous stomatitis.

K. Cachexia
Authorization of 12 months may be granted for treatment of cachexia caused by cancer or HIV-infection.

L. HIV-associated Diarrhea
Authorization of 12 months may be granted for treatment of HIV-associated diarrhea.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

TIBSOVO (ivosidenib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Newly-Diagnosed Acute Myeloid Leukemia
   Tibsovo is indicated for the treatment of newly-diagnosed acute myeloid leukemia (AML) with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test in adult patients who are ≥ 75 years old or who have comorbidities that preclude use of intensive induction chemotherapy.

2. Relapsed or Refractory Acute Myeloid Leukemia
   Tibsovo is indicated for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test.

B. Compendial Uses

Tibsovo is used as a single agent in patients age ≥ 60 years with IDH1-mutated AML in the following settings:

1. Treatment induction when not a candidate for intensive remission induction therapy or declines intensive therapy OR
2. Post-remission therapy following response to previous lower intensity therapy with the same regimen

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Newly-Diagnosed Acute Myeloid Leukemia
   Authorization of 12 months may be granted for treatment of newly-diagnosed acute myeloid leukemia with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation as monotherapy when any of the following criteria is met:
   1. The member has comorbidities that preclude use of intensive induction chemotherapy, or
   2. The member is 60 years of age or older and is not a candidate for intensive remission induction therapy or declines intensive therapy.

B. Relapsed or Refractory Acute Myeloid Leukemia
   Authorization of 12 months may be granted for members for treatment of relapsed or refractory acute myeloid leukemia with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation as monotherapy.
C. Post-remission Therapy for Acute Myeloid Leukemia

Authorization of 12 months may be granted for members for treatment of acute myeloid leukemia with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation for members who are 60 years of age or older and who are using Tibsovo as monotherapy for post-remission therapy following response to previous lower intensity therapy with the same regimen.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCE

SPECIALTY GUIDELINE MANAGEMENT

**tobramycin inhalation solution/TOBI**
TOBI Podhaler (tobramycin inhalation powder)
Bethkis (tobramycin inhalation solution)
Kitabis Pak (tobramycin inhalation solution)

**POLICY**

I. **INDICATIONS**

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

   Management of cystic fibrosis in patients with *Pseudomonas aeruginosa*

B. Compendial Uses

   *Pseudomonas aeruginosa* lower respiratory tract infection in patients with non-cystic fibrosis bronchiectasis

All other indications are considered experimental/investigational and are not a covered benefit.

II. **CRITERIA FOR INITIAL APPROVAL**

A. Cystic Fibrosis

   Authorization of 24 months may be granted for members with cystic fibrosis when *Pseudomonas aeruginosa* is present in airway cultures OR the member has a history of *Pseudomonas aeruginosa* infection or colonization in the airways.

B. Bronchiectasis (Non-Cystic Fibrosis)

   Authorization of 24 months may be granted for members with non-cystic fibrosis bronchiectasis when *Pseudomonas aeruginosa* is present in airway cultures OR the member has a history of *Pseudomonas aeruginosa* infection or colonization in the airways.

III. **CONTINUATION OF THERAPY**

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. **REFERENCES**


SPECIALTY GUIDELINE MANAGEMENT

TORISEL (temsirolimus)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
   Advanced renal cell carcinoma

B. Compendial Uses
   1. Relapsed or surgically unresectable stage IV kidney cancer
   2. Endometrial carcinoma
   3. Soft tissue sarcoma subtypes:
      a. Perivascular epithelioid cell tumors (PEComa)
      b. Recurrent angiomyolipoma
      c. Lymphangioleiomyomatosis

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Renal Cell Carcinoma (RCC)
   Authorization of 12 months may be granted for treatment of relapsed, metastatic, or unresectable RCC.

B. Endometrial Carcinoma
   Authorization of 12 months may be granted for single-agent treatment of endometrial carcinoma.

C. Soft Tissue Sarcoma
   Authorization of 12 months may be granted for treatment of soft tissue sarcoma with any of the following subtypes: perivascular epithelioid cell tumor (PEComa), recurrent angiomyolipoma, or lymphangioleiomyomatosis.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in Section II when there is no evidence of unacceptable toxicity or disease progression on the current regimen.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

TREANDA (bendamustine)
BENDEKA (bendamustine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Chronic lymphocytic leukemia (CLL)
   2. Indolent B-cell non-Hodgkin lymphoma (NHL) that has progressed during or within six months of treatment with rituximab or a rituximab-containing regimen

B. Compendial Uses
   1. Classical Hodgkin lymphoma (CHL)
   2. Multiple myeloma (MM)
   3. Non-Hodgkin lymphoma (NHL)
      i. Adult T-cell leukemia/lymphoma (ATLL)
      ii. Acquired immune deficiency syndrome (AIDS)-related B-cell lymphoma
      iii. CLL/small lymphocytic lymphoma (SLL)
      iv. Diffuse large B-cell lymphoma (DLBCL)
      v. Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma
      vi. Histologic transformation of follicular lymphoma to diffuse large B-cell lymphoma
      vii. High grade B-cell lymphoma
      viii. Follicular lymphoma
      ix. Marginal zone lymphoma
         a. Nodal marginal zone lymphoma
         b. Gastric mucosa associated lymphoid tissue (MALT) lymphoma
         c. Nongastric MALT lymphoma
         d. Splenic marginal zone lymphoma
      x. Mantle cell lymphoma (MCL)
     xi. Mycosis fungoides (MF)/Sezary syndrome (SS)
     xii. Peripheral T-cell lymphoma (PTCL)
     xiii. Primary cutaneous B-cell lymphoma
     xiv. Primary cutaneous CD30+ T-cell lymphoproliferative disorder: cutaneous anaplastic large cell lymphoma (ALCL)
     xv. Post-transplant lymphoproliferative disorders
     xvi. Hepatosplenic Gamma-Delta T-Cell lymphoma
     4. Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma
     5. Small cell lung cancer

All other indications are considered experimental/investigational and are not a covered benefit.
II. CRITERIA FOR INITIAL APPROVAL

A. Non-Hodgkin lymphoma (NHL)
   Authorization of 12 months may be granted for treatment of NHL with any of the following subtypes:
   1. Follicular lymphoma
   2. Chronic lymphocytic leukemia/small lymphocytic leukemia (CLL/SLL) without chromosome 17p deletion or TP53 mutation
   3. High-grade B-cell lymphoma when both of following are met:
      a. The requested agent is used as second-line or subsequent therapy, and
      b. The patient is not a candidate for transplant.
   4. Diffuse large B-cell lymphoma (DLBCL) when both of the following are met:
      a. The requested agent is used as second-line or subsequent therapy, and
      b. The patient is not a candidate for transplant.
   5. Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma when the patient has received at least two chemoimmunotherapy regimens.
   6. Histologic transformation of follicular lymphoma to diffuse large B-cell lymphoma when the patient has received at least two chemoimmunotherapy regimens.
   7. Adult T-cell leukemia/lymphoma (ATLL) when both of the following are met:
      a. The requested agent is used as a single agent, and
      b. The requested agent is used as second-line or subsequent therapy.
   8. AIDS-related B-cell lymphoma when both of the following are met:
      a. The requested agent is used as second-line or subsequent therapy, and
      b. The patient is not a candidate for transplant.
   9. Marginal zone lymphoma
      a. Nodal marginal zone lymphoma when used in combination with rituximab or obinutuzumab.
      b. Gastric MALT lymphoma when used in combination with rituximab or obinutuzumab.
      c. Nongastric MALT lymphoma when used in combination with rituximab or obinutuzumab.
      d. Splenic marginal zone lymphoma when used in combination with rituximab or obinutuzumab.
   10. Mantle cell lymphoma (MCL) when either of the following are met:
       a. The requested agent is used as a single agent, or
       b. The requested agent is used in combination with rituximab.
   11. Mycosis fungoides (MF)/Sezary syndrome (SS)
   12. Peripheral T-cell lymphoma (PTCL) when both of the following are met:
       a. The requested agent is used as a single agent, and
       b. The requested agent is used as second-line or subsequent therapy.
   13. Primary cutaneous B-cell lymphoma when both of the following are met:
       a. The requested agent is used as second-line or subsequent therapy.
       b. The patient is not a candidate for transplant.
   14. Cutaneous anaplastic large cell lymphoma (ALCL) when both of the following are met:
       a. The requested agent is used as a single agent, and
       b. The requested agent is used for relapsed or refractory disease.
   15. Post-transplant lymphoproliferative disorders when used as second-line or subsequent therapy.
   16. Hepatosplenic gamma-delta T-Cell lymphoma when both of the following are met:
       a. The requested agent is used as a single agent, and
       b. The requested agent is used for refractory disease.

B. Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma
   Authorization of 12 months may be granted for treatment of Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma when either of the following are met
   1. The requested agent will be used in combination with rituximab, or
   2. The requested agent will be used as a single agent.
C. Multiple myeloma (MM)

Authorization of 12 months may be granted for treatment of MM when both of the following criteria are met:

1. The disease is relapsed or progressive, and
2. The requested agent will be used in any of the following regimens:
   a. In combination with lenalidomide and dexamethasone, or
   b. In combination with bortezomib and dexamethasone, or
   c. As a single agent.

D. Classical Hodgkin lymphoma (CHL)

Authorization of 12 months may be granted for treatment of CHL when both of the following criteria are met:

1. The requested agent will be used as second line, subsequent therapy, or palliative therapy, and
2. The requested agent will be used in any of the following regimens:
   a. In combination with brentuximab vedotin, or
   b. In combination with gemcitabine and vinorelbine, or
   c. As a single agent.

E. Small cell lung cancer (SCLC)

Authorization of 12 months may be granted for treatment of SCLC when both of the following criteria are met:

1. The requested agent is being used for subsequent therapy, and
2. The requested agent will be used as a single agent.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

TRELSTAR (triptorelin pamoate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
   Palliative treatment of advanced prostate cancer

B. Compendial Uses
   1. Prostate cancer
   2. Gender dysphoria (also known as gender non-conforming or transgender persons)
      NOTE: Some plans may opt-out of coverage for gender dysphoria.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Prostate cancer
   Authorization of 12 months may be granted for treatment of prostate cancer.

B. Gender dysphoria
   1. Authorization of 12 months may be granted for pubertal suppression in preparation for gender reassignment in an adolescent member when all of the following criteria are met:
      a. The member has a diagnosis of gender dysphoria.
      b. The member has reached Tanner stage 2 of puberty.
   2. Authorization of 12 months may be granted for gender reassignment in an adult member when all of the following criteria are met:
      a. The member has a diagnosis of gender dysphoria.
      b. The member will receive Trelstar concomitantly with cross sex hormones.

III. CONTINUATION OF THERAPY

   All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

TREMFYA (guselkumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Treatment of adult patients with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Moderate to severe plaque psoriasis
A. Authorization of 24 months may be granted for members who are 18 years of age or older who have previously received Tremfya, Otezla, or any other biologic DMARD indicated for the treatment of moderate to severe plaque psoriasis.

B. Authorization of 24 months may be granted for treatment of moderate to severe plaque psoriasis for members who are 18 years of age or older when all of the following criteria are met:
   1. At least 5% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
   2. Member meets any of the following criteria:
      a. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
      b. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine or acitretin (see Appendix).
      c. Member has severe psoriasis that warrants a biologic DMARD as first-line therapy.

III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 4 months of therapy with Tremfya as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB).

Note: Members who have received Tremfya or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) are exempt from requirements related to TB screening in this Policy.
V. APPENDIX

Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin
1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Cannot be used due to risk of treatment-related toxicity
4. Drug interaction
5. Pregnancy or planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VI. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

Remodulin injection (treprostinil injection)
treprostinil injection (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. **Pulmonary Arterial Hypertension**
   Remodulin is indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to diminish symptoms associated with exercise.

2. **Pulmonary Arterial Hypertension in Patients Requiring Transition from Epoprostenol**
   In patients with PAH requiring transition from epoprostenol, Remodulin is indicated to diminish the rate of clinical deterioration. Consider the risks and benefits of each drug prior to transition.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Indefinite authorization may be granted for treatment of PAH when ALL of the following criteria are met:

A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).

B. PAH was confirmed by either criterion (1) or criterion (2) below:
   1. Pretreatment right heart catheterization with all of the following results:
      i. mPAP ≥ 25 mmHg
      ii. PCWP ≤ 15 mmHg
      iii. PVR > 3 Wood units
   2. For infants less than one year of age with any of the following conditions, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed:
      i. Post cardiac surgery
      ii. Chronic heart disease
      iii. Chronic lung disease associated with prematurity
      iv. Congenital diaphragmatic hernia

III. CONTINUATION OF THERAPY

Indefinite authorization may be granted for members with an indication listed in Section II who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. APPENDIX
WHO Classification of Pulmonary Hypertension

1 PAH
1.1 Idiopathic (PAH)
1.2 Heritable PAH
1.3 Drug- and toxin-induced PAH
1.4 PAH associated with:
   1.4.1 Connective tissue diseases
   1.4.2 HIV infection
   1.4.3 Portal hypertension
   1.4.4 Congenital heart diseases
   1.4.5 Schistosomiasis
1.5 PAH long-term responders to calcium channel blockers
1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease
2.1 PH due to heart failure with preserved LVEF
2.2 PH due to heart failure with reduced LVEF
2.3 Valvular heart disease
2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia
3.1 Obstructive lung disease
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction
4.1 Chronic thromboembolic PH
4.2 Other pulmonary artery obstructions
   4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
   4.2.2 Other malignant tumors
       Renal carcinoma
       Uterine carcinoma
       Germ cell tumours of the testis
       Other tumours
   4.2.3 Non-malignant tumours
       Uterine leiomyoma
   4.2.4 Arteritis without connective tissue disease
   4.2.5 Congenital pulmonary artery stenosis
   4.2.6 Parasites
       Hydatidosis

5 PH with unclear and/or multifactorial mechanisms
5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
5.4 Complex congenital heart disease

V. REFERENCES
PRIOR AUTHORIZATION CRITERIA

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Status: CVS Caremark Criteria Ref # 237-A
Type: Initial Prior Authorization Ref # 355-A

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS
Atralin, Avita, Retin-A, Retin-A Micro, Tretin-X are indicated for topical application in the treatment of acne vulgaris. The safety and efficacy of these products in the treatment of other disorders have not been established. Veltin and Ziana are indicated for the topical treatment of acne vulgaris in patients 12 years or older. Altreno (tretinoin) lotion, 0.05% is indicated for the topical treatment of acne vulgaris in patients 9 years of age and older.

Compendial Use
Keratosis follicularis (Darier's disease, Darier-White disease) 12, 15, 16

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:
- The patient has the diagnosis of acne vulgaris or keratosis follicularis (Darier's disease, Darier-White disease)
RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Tretinoins are indicated for the topical treatment of acne vulgaris. The safety and efficacy of these products in the treatment of other disorders have not been established. The criteria do not provide for cosmetic uses of these drugs.

The American Academy of Dermatology guidelines state that the topical therapy of acne vulgaris includes the usage of agents that are available over the counter or via prescription. Therapy choice may be influenced by age of the patient, site of involvement, extent and severity of disease, and patient preference. Topical therapies may be used as monotherapy, in combination with other topical agents or in combination with oral agents in both initial control and maintenance. Topical retinoids are important in addressing the development and maintenance of acne and are recommended as monotherapy in primarily comedonal acne, or in combination with topical or oral antimicrobials in patients with mixed or primarily inflammatory acne lesions. Commonly used topical acne therapies include benzoyl peroxide, salicylic acid, antibiotics, combination antibiotics with benzoyl peroxide, retinoids, retinoid with benzoyl peroxide, retinoid with antibiotic, azelaic acid, and sulfone agents.14

Topical tretinoin has been used for the treatment of keratosis follicularis.12 Moisturizers with urea or lactic acid can help reduce scaling and thickening of the lesions, low to medium potency topical steroids are sometimes useful for reducing inflammation, and when bacterial growth is suspected, application of antiseptics can be helpful. Topical retinoids also may reduce hyperkeratosis within three months.15, 16

Renova and Refissa are indicated as adjunctive agents for use in the mitigation of fine facial wrinkles in patients who use comprehensive skin care and sunlight avoidance programs.5–6 Since the treatment of these indications is considered cosmetic, these two tretinoin products are not included in the criteria.

REFERENCES

CRITERIA FOR APPROVAL

1. Does the patient have the diagnosis of acne vulgaris?  
   Yes  No  
   [If yes, then no further questions.]

2. Does the patient have the diagnosis of keratosis follicularis (Darier’s disease, Darier-White disease)?  
   Yes  No

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Clinical changes: 08/2018 (Added Altreno), 06/2019 (separated diagnoses questions; combined 237-A [removed MDC designation and applied compendial use to 237-A])

Reviewed:  
# PRIOR AUTHORIZATION CRITERIA

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**Status:** CVS Caremark Criteria  
**Type:** Initial Prior Authorization  
**MMT Ref # 904-A**

*Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

## FDA-APPROVED INDICATIONS

Atralin, Avita, Retin-A, Retin-A Micro, Tretin-X are indicated for topical application in the treatment of acne vulgaris. The safety and efficacy of these products in the treatment of other disorders have not been established.

Veltin and Ziana are indicated for the topical treatment of acne vulgaris in patients 12 years or older.

Altreno (tretinoin) lotion, 0.05% is indicated for the topical treatment of acne vulgaris in patients 9 years of age and older.

Compendial Use
Keratosis follicularis (Darier’s disease, Darier-White disease)\(^{12,15,16}\)

## COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has the diagnosis of keratosis follicularis (Darier’s disease, Darier-White disease)
OR
• The patient has the diagnosis of acne vulgaris AND experienced an inadequate treatment response, an intolerance, or contraindication to benzoyl peroxide

RATIONALE
The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Tretinoins are indicated for the topical treatment of acne vulgaris. The safety and efficacy of these products in the treatment of other disorders have not been established. The criteria do not provide for cosmetic uses of these drugs.

Benzoyl peroxide is a bactericidal agent that has proven effective in the treatment of acne vulgaris and is the most widely studied OTC medication. It is safe and may be used as a monotherapy or in combination with other topical medications for mild acne, and is part of the regimen of care applied to acne of all severities and types. Its use may also minimize the development of antibiotic-resistant Propionibacterium acnes when used in combination with systemic or topical antibiotics. The American Academy of Dermatology guidelines state that the topical therapy of acne vulgaris includes the usage of agents that are available over the counter or via prescription. Therapy choice may be influenced by age of the patient, site of involvement, extent and severity of disease, and patient preference. Topical therapies may be used as monotherapy, in combination with other topical agents or in combination with oral agents in both initial control and maintenance. Commonly used topical acne therapies include benzoyl peroxide, salicylic acid, antibiotics, combination antibiotics with benzoyl peroxide, retinoids, retinoid with benzoyl peroxide, retinoid with antibiotic, azelaic acid, and sulfone agents.

Topical tretinoin has been used for the treatment of keratosis follicularis. Moisturizers with urea or lactic acid can help reduce scaling and thickening of the lesions, low to medium potency topical steroids are sometimes useful for reducing inflammation, and when bacterial growth is suspected, application of antiseptics can be helpful. Topical retinoids also may reduce hyperkeratosis within three months.

Renova and Refissa are indicated as adjunctive agents for use in the mitigation of fine facial wrinkles in patients who use comprehensive skin care and sunlight avoidance programs. Since the treatment of these indications is considered cosmetic, these two tretinoin products are not included in the criteria.

REFERENCES
CRITERIA FOR APPROVAL

1. Does the patient have the diagnosis of acne vulgaris?  
   [If no, then skip to question 3.]  
   Yes  No

2. Has the patient experienced an inadequate treatment response, an intolerance, or contraindication to benzoyl peroxide?  
   [No further questions.]  
   Yes  No

3. Does the patient have the diagnosis of keratosis follicularis (Darier’s disease, Darier-White disease)?  
   Yes  No

Mapping Instructions

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DENIAL REASONS – DO NOT USE FOR MEDICARE PART D

- You do not meet the requirements of your plan.  
- Your plan covers this drug when you have tried benzoyl peroxide and it did not work for you, or you cannot use it.  
- Your request has been denied based on the information we have.  
- [Short Description: No inadequate treatment response, an intolerance, or contraindication to benzoyl peroxide.]

- You do not meet the requirements of your plan.  
- Your plan covers this drug when you have any of these conditions:  
  - Acne vulgaris  
  - Keratosis follicularis (Darier’s disease, Darier-White disease)  
- Your request has been denied based on the information we have.  
- [Short Description: No approvable diagnosis.]
SPECIALTY GUIDELINE MANAGEMENT

TRIPTODUR (triptorelin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Triptodur is indicated for the treatment of pediatric patients 2 years of age and older with central precocious puberty (CPP).

B. Compendial Use

Gender dysphoria (also known as gender non-conforming or transgender persons)

NOTE: Some plans may opt-out of coverage for gender dysphoria.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Central precocious puberty (CPP)

1. Authorization up to age 12 may be granted for the treatment of CPP in a female member when all of the following criteria are met:
   a. The diagnosis of CPP has been confirmed by a pubertal response to a gonadotropin releasing hormone (GnRH) agonist test or a pubertal level of a third generation luteinizing hormone (LH) assay.
   b. The assessment of bone age versus chronological age supports the diagnosis of CPP.
   c. The member was less than 8 years of age at the onset of secondary sexual characteristics.

2. Authorization up to age 13 may be granted for the treatment of CPP in a male member when all of the following criteria are met:
   a. The diagnosis of CPP has been confirmed by a pubertal response to a GnRH agonist test or a pubertal level of a third generation LH assay.
   b. The assessment of bone age versus chronological age supports the diagnosis of CPP.
   c. The member was less than 9 years of age at the onset of secondary sexual characteristics.

B. Gender dysphoria

1. Authorization of 12 months may be granted for pubertal suppression in preparation for gender reassignment in an adolescent member when all of the following criteria are met:
   a. The member has a diagnosis of gender dysphoria.
   b. The member has reached Tanner stage 2 of puberty.

2. Authorization of 12 months may be granted for gender reassignment in an adult member when all of the following criteria are met:
   a. The member has a diagnosis of gender dysphoria.
   b. The member will receive Triptodur concomitantly with cross sex hormones.
III. CONTINUATION OF THERAPY

A. Central precocious puberty (CPP)
   1. Authorization up to age 12 may be granted for continuation of therapy for CPP in a female member if the member is currently less than 12 years of age.
   2. Authorization up to age 13 may be granted for continuation of therapy for CPP in a male member if the member is currently less than 13 years of age.

B. Gender Dysphoria
   All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

TURALIO (pexidartinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Turalio is indicated for the treatment of adult patients with symptomatic tenosynovial giant cell tumor (TGCT) associated with severe morbidity or functional limitations and not amendable to improvement with surgery.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Symptomatic Tenosynovial Giant Cell Tumor

Authorization of 12 months may be granted for the treatment of symptomatic tenosynovial giant cell tumor (TGCT) associated with severe morbidity or functional limitations and that is not amenable to improvement with surgery.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced an unacceptable toxicity or disease progression.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

TYKERB (lapatinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
Tykerb is indicated in combination with:
1. Capecitabine for the treatment of patients with advanced or metastatic breast cancer whose tumors overexpress human epidermal growth factor receptor 2 (HER2) and who have received prior therapy including an anthracycline, a taxane, and trastuzumab
2. Letrozole for the treatment of postmenopausal women with hormone receptor (HR)-positive metastatic breast cancer that overexpresses the HER2 receptor for whom hormonal therapy is indicated

B. Compendial Uses
1. Recurrent or metastatic HER2-positive breast cancer in combination with trastuzumab
2. Recurrent or stage IV hormone receptor-positive, HER2-positive breast cancer in combination with aromatase inhibition in postmenopausal women
3. Metastatic central nervous system (CNS) lesions if active against primary tumor (breast)
4. Recurrent EGFR-positive chordoma

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Breast cancer
Authorization of 12 months may be granted for the treatment of HER2-positive breast cancer when Tykerb is used in combination with an aromatase inhibitor (e.g., letrozole, anastrozole, exemestane), trastuzumab, or capecitabine.

B. Metastatic CNS lesions
Authorization of 12 months may be granted for the treatment of metastatic CNS lesions from HER2-positive breast cancer.

C. Chordoma
Authorization of 12 months may be granted for the treatment of EGFR-positive recurrent chordoma.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.
IV. REFERENCES

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Tymlos is indicated for the treatment postmenopausal women with osteoporosis at high risk for fracture defined as history of osteoporotic fracture, multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy.

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Supporting chart notes or medical record indicating a history of fractures, T-score, and FRAX fracture probability as applicable to section III.

III. CRITERIA FOR APPROVAL

Postmenopausal osteoporosis
Authorization of a lifetime total of 24 months for parathyroid hormone analogs (e.g., abaloparatide or teriparatide) may be granted to postmenopausal members with osteoporosis when ANY of the following criteria are met:
A. Member has a history of fragility fractures
B. Member has a pre-treatment T-score less than or equal to -2.5 OR member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B) and meets ANY of the following criteria:
   1. Member has indicators of higher fracture risk (e.g., advanced age, frailty, glucocorticoid use, very low T-scores [less than or equal to -3.5], or increased fall risk)
   2. Member has failed prior treatment with or is intolerant to previous injectable osteoporosis therapy (e.g., zoledronic acid [Reclast], denosumab [Prolia])
   3. Member has had an oral bisphosphonate trial of at least 1-year duration or there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet ALL
initial authorization criteria AND have received less than 24 months of total lifetime therapy with parathyroid hormone analogs (e.g., abaloparatide or teriparatide).

V. APPENDIX

Appendix A. Clinical reasons to avoid oral bisphosphonate therapy
- Esophageal abnormality that delays emptying such as stricture of achalasia
- Active upper gastrointestinal problem (e.g., dysphagia, gastritis, duodenitis, erosive esophagitis, ulcers)
- Inability to stand or sit upright for at least 30 to 60 minutes
- Inability to take at least 30 to 60 minutes before first food, drink, or medication of the day
- Renal insufficiency (creatinine clearance < 35 mL/min)
- History of intolerance to an oral bisphosphonate

Appendix B. WHO Fracture Risk Assessment Tool
- High FRAX fracture probability: 10 year major osteoporotic fracture risk ≥ 20% or hip fracture risk ≥ 3%.
- 10-year probability; calculation tool available at: https://www.sheffield.ac.uk/FRAX/
- The estimated risk score generated with FRAX should be multiplied by 1.15 for major osteoporotic fracture and 1.2 for hip fracture if glucocorticoid treatment is greater than 7.5 mg per day.

VI. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

TYSABRI (natalizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
A. Moderately to severely active Crohn’s disease (CD)
B. Monotherapy for the treatment of relapsing forms of multiple sclerosis, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

All other indications are considered experimental/investigational and are not a covered benefit.

II. EXCLUSIONS

Members will not use Tysabri concomitantly with other medications used for the treatment of multiple sclerosis, excluding Ampyra. Member is anti-JCV antibody testing positive.

III. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active Crohn’s disease (CD)
   1. Authorization of 24 months may be granted to members who have received Tysabri or any other biologic indicated for the treatment of Crohn’s disease.
   2. Authorization of 24 months may be granted for members who have an inadequate response, intolerance or contraindication to BOTH of the following:
      a. At least ONE conventional therapy option (See Appendix)
      b. At least ONE TNF-alpha inhibitor indicated for CD:
         i. Cimzia (certolizumab)
         ii. Humira (adalimumab)
         iii. Remicade (infliximab)

B. Relapsing forms of multiple sclerosis (MS)
   Authorization of 12 months may be granted to members who have been diagnosed with a relapsing forms of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

C. Clinically isolated syndrome
   Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome of multiple sclerosis.
IV. CONTINUATION OF THERAPY

A. Crohn’s disease
Authorization of 24 months may be granted for all members (including new members) who meet ALL initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Tysabri as evidenced by low disease activity or improvement in signs and symptoms of the condition.

B. Multiple sclerosis (MS) including relapsing forms of MS and clinically isolated syndrome
Authorization of 12 months may be granted for all members (including new members) who achieve or maintain a positive clinical response with Tysabri as evidenced by experiencing disease stability or improvement.

V. APPENDIX

Examples of Conventional Therapy Options for CD
1. Mild to moderate disease – induction of remission:
   a. Oral budesonide
   b. Alternatives: metronidazole, ciprofloxacin, rifaximin
2. Mild to moderate disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternatives: oral budesonide, methotrexate intramuscular (IM) or subcutaneous (SC), sulfasalazine
3. Moderate to severe disease – induction of remission:
   a. Prednisone, methylprednisolone intravenously (IV)
   b. Alternatives: methotrexate IM or SC
4. Moderate to severe disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: methotrexate IM or SC
5. Perianal and fistulizing disease – induction of remission
   a. Metronidazole ± ciprofloxacin, tacrolimus
6. Perianal and fistulizing disease – maintenance of remission
   a. Azathioprine, mercaptopurine
   b. Alternative: methotrexate IM or SC

VI. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

Tyvaso (treprostinil inhalation solution)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Tyvaso is indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise ability.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:

A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
B. PAH was confirmed by either criterion (1) or criterion (2) below:
   1. Pretreatment right heart catheterization with all of the following results:
      i. mPAP ≥ 25 mmHg
      ii. PCWP ≤ 15 mmHg
      iii. PVR > 3 Wood units
   2. For infants less than one year of age with any of the following conditions, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed:
      i. Post cardiac surgery
      ii. Chronic heart disease
      iii. Chronic lung disease associated with prematurity
      iv. Congenital diaphragmatic hernia

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section II who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. APPENDIX

WHO Classification of Pulmonary Hypertension

1 PAH
   1.1 Idiopathic (PAH)
   1.2 Heritable PAH
   1.3 Drug- and toxin-induced PAH
1.4. PAH associated with:
   1.4.1 Connective tissue diseases
   1.4.2 HIV infection
   1.4.3 Portal hypertension
   1.4.4 Congenital heart diseases
   1.4.5 Schistosomiasis

1.5 PAH long-term responders to calcium channel blockers

1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement

1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease
2.1 PH due to heart failure with preserved LVEF
2.2 PH due to heart failure with reduced LVEF
2.3 Valvular heart disease
2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia
3.1 Obstructive lung disease
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction
4.1 Chronic thromboembolic PH
4.2 Other pulmonary artery obstructions
   4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
   4.2.2 Other malignant tumors
      Renal carcinoma
      Uterine carcinoma
      Germ cell tumours of the testis
      Other tumours
   4.2.3 Non-malignant tumours
      Uterine leiomyoma
   4.2.4 Arteritis without connective tissue disease
   4.2.5 Congenital pulmonary artery stenosis
   4.2.6 Parasites
      Hydatidosis

5 PH with unclear and/or multifactorial mechanisms
5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
5.4 Complex congenital heart disease

V. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT
ULTOMIRIS (ravulizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Ultomiris is indicated for the treatment of adult patients with paroxysmal nocturnal hemoglobinuria.

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review for new requests for treatment of paroxysmal nocturnal hemoglobinuria: deficiency of glycosylphosphatidylinositol (GPI)-anchored proteins, flow cytometry used to show results of GPI-APs deficiency

III. CRITERIA FOR INITIAL APPROVAL

Paroxysmal nocturnal hemoglobinuria
Authorization of 6 months may be granted for treatment of paroxysmal nocturnal hemoglobinuria when all of the following criteria are met:
A. Deficiency of glycosylphosphatidylinositol-anchored proteins (GPI-APs)
B. Flow cytometry is used to demonstrate GPI-APs deficiency

IV. CONTINUATION OF THERAPY

Paroxysmal nocturnal hemoglobinuria
Authorization of 12 months may be granted to all members (including new members) requesting continuation of therapy provided they meet all initial authorization criteria and demonstrate a positive response to therapy (e.g., improvement in hemoglobin levels, normalization of LDH levels).

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

Uptravi (selexipag)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Uptravi is indicated for the treatment of pulmonary arterial hypertension (PAH, WHO Group I) to delay disease progression and reduce the risk of hospitalization for PAH.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:

A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix)

B. PAH was confirmed by either criterion (1) or criterion (2) below:

1. Pretreatment right heart catheterization with all of the following results:
   i. mPAP ≥ 25 mmHg
   ii. PCWP ≤ 15 mmHg
   iii. PVR > 3 Wood units

2. For infants less than one year of age with any of the following conditions, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed:
   i. Post cardiac surgery
   ii. Chronic heart disease
   iii. Chronic lung disease associated with prematurity
   iv. Congenital diaphragmatic hernia

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section II who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. APPENDIX

WHO Classification of Pulmonary Hypertension

1 PAH
   1.1 Idiopathic (PAH)
   1.2 Heritable PAH
   1.3 Drug- and toxin-induced PAH
   1.4. PAH associated with:
1.4.1 Connective tissue diseases
1.4.2 HIV infection
1.4.3 Portal hypertension
1.4.4 Congenital heart diseases
1.4.5 Schistosomiasis
1.5 PAH long-term responders to calcium channel blockers
1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease
2.1 PH due to heart failure with preserved LVEF
2.2 PH due to heart failure with reduced LVEF
2.3 Valvular heart disease
2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia
3.1 Obstructive lung disease
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction
4.1 Chronic thromboembolic PH
4.2 Other pulmonary artery obstructions
  4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
  4.2.2 Other malignant tumors
    Renal carcinoma
    Uterine carcinoma
    Germ cell tumours of the testis
    Other tumours
  4.2.3 Non-malignant tumours
    Uterine leiomyoma
  4.2.4 Arteritis without connective tissue disease
  4.2.5 Congenital pulmonary artery stenosis
  4.2.6 Parasites
    Hydatidosis

5 PH with unclear and/or multifactorial mechanisms
5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
5.4 Complex congenital heart disease

V. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

VALCHLOR (mechlorethamine gel)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. **FDA-Approved Indications**

Valchlor is indicated for the topical treatment of Stage IA and IB mycosis fungoides-type cutaneous T-cell lymphoma in patients who have received prior skin-directed therapy.

B. **Compendial Uses**

1. Chronic or smoldering adult T-cell leukemia/lymphoma
2. Mycosis fungoides/Sezary syndrome
3. Primary cutaneous B-cell lymphoma:
   a. Primary cutaneous marginal zone lymphoma
   b. Primary cutaneous follicle center lymphoma
4. Lymphomatoid papulosis

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. **Mycosis Fungoides/Sezary Syndrome**

Authorization of 12 months may be granted for the treatment of mycosis fungoides or Sezary syndrome.

B. **Adult T-cell leukemia/lymphoma**

Authorization of 12 months may be granted for the treatment of chronic or smoldering adult T-cell leukemia/lymphoma.

C. **Primary cutaneous B-cell lymphoma**

Authorization of 12 months may be granted for the treatment of primary cutaneous marginal zone or follicle center lymphoma.

D. **Lymphomatoid Papulosis**

Authorization of 12 months may be granted for the treatment of lymphomatoid papulosis.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria.
IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

VANTAS (histrelin acetate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
   Palliative treatment of advanced prostate cancer

B. Compendial Uses
   1. Prostate cancer
   2. Gender dysphoria (also known as gender non-conforming or transgender persons)

   NOTE: Some plans may opt-out of coverage for gender dysphoria.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Prostate cancer
   Authorization of 12 months may be granted for treatment of prostate cancer.

B. Gender dysphoria
   1. Authorization of 12 months may be granted for pubertal suppression in preparation for gender reassignment in an adolescent member when all of the following criteria are met:
      a. The member has a diagnosis of gender dysphoria.
      b. The member has reached Tanner stage 2 of puberty.
   2. Authorization of 12 months may be granted for gender reassignment in an adult member when all of the following criteria are met:
      a. The member has a diagnosis of gender dysphoria.
      b. The member will receive Vantas concomitantly with cross sex hormones.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

VECTIBIX (panitumumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Vectibix is indicated for the treatment of patients with wild-type RAS (defined as wild-type in both KRAS and NRAS as determined by an FDA-approved test for this use) metastatic colorectal cancer (mCRC):

1. As first-line therapy in combination with FOLFOX (fluorouracil, leucovorin, and oxaliplatin)
2. As monotherapy following disease progression after prior treatment with fluoropyrimidine-, oxaliplatin-,

and irinotecan-containing chemotherapy

Limitation of Use: Vectibix is not indicated for the treatment of patients with RAS-mutant mCRC or for whom RAS mutation status is unknown.

B. Compendial Use

Colorectal cancer

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Colorectal Cancer (CRC)

Authorization of 12 months may be granted for the treatment of colorectal cancer when all of the following criteria are met:

A. The RAS (KRAS and NRAS) mutation status is negative (wild-type).
B. Member has not previously experienced clinical failure on cetuximab.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

VEMLIDY (tenofovir alafenamide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Treatment of chronic hepatitis B virus (HBV) infection in adults with compensated liver disease

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Chronic hepatitis B virus infection
Authorization of 6 months may be granted for treatment of chronic hepatitis B virus (HBV) when the member is HIV-1 negative.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

VENCLEXTA (venetoclax)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Venclexta is indicated for the treatment of patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).
   2. Venclexta is indicated in combination with azacitidine, or decitabine, or low-dose cytarabine for the treatment of newly-diagnosed acute myeloid leukemia (AML) in adults who are age 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy.

B. Compendial Uses
   1. Mantle cell lymphoma
   2. In combination with rituximab for relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) in patients who have indications for treatment

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL)
   Authorization of 12 months may be granted for treatment of chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL).

B. Newly-diagnosed Acute Myeloid Leukemia (AML)
   Authorization of 12 months may be granted for treatment of newly-diagnosed acute myeloid leukemia (AML) when any of the following criteria is met:
   1. The member is 75 years of age or older.
   2. The member has comorbidities that preclude treatment with intensive induction chemotherapy.

C. Mantle Cell Lymphoma
   Authorization of 12 months may be granted for treatment of mantle cell lymphoma.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

Ventavis (iloprost inhalation solution)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Ventavis is indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve a composite endpoint consisting of exercise tolerance, symptoms (NYHA Class), and lack of deterioration.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:
A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
B. PAH was confirmed by either criterion (1) or criterion (2) below:
   1. Pretreatment right heart catheterization with all of the following results:
      i. mPAP ≥ 25 mmHg
      ii. PCWP ≤ 15 mmHg
      iii. PVR > 3 Wood units
   2. For infants less than one year of age with any of the following conditions, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed:
      i. Post cardiac surgery
      ii. Chronic heart disease
      iii. Chronic lung disease associated with prematurity
      iv. Congenital diaphragmatic hernia

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section II who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. APPENDIX

WHO Classification of Pulmonary Hypertension
1 PAH
1.1 Idiopathic (PAH)
1.2 Heritable PAH
1.3 Drug- and toxin-induced PAH
1.4. PAH associated with:
   1.4.1 Connective tissue diseases
   1.4.2 HIV infection
   1.4.3 Portal hypertension
   1.4.4 Congenital heart diseases
   1.4.5 Schistosomiasis
1.5 PAH long-term responders to calcium channel blockers
1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
1.7 Persistent PH of the newborn syndrome

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3.4 Hypoxia without lung disease
3.5 Developmental lung disorders

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4.1 Chronic thromboembolic PH
4.2 Other pulmonary artery obstructions
   4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
   4.2.2 Other malignant tumors
      Renal carcinoma
      Uterine carcinoma
      Germ cell tumours of the testis
      Other tumours
   4.2.3 Non-malignant tumours
      Uterine leiomyoma
   4.2.4 Arteritis without connective tissue disease
   4.2.5 Congenital pulmonary artery stenosis
   4.2.6 Parasites
      Hydatidosis

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5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
5.4 Complex congenital heart disease

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

VERZENIO (abemaciclib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Verzenio is indicated:

A. In combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer.

B. In combination with fulvestrant for the treatment of women with HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression following endocrine therapy.

C. As monotherapy for the treatment of adult patients with HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression following endocrine therapy and prior chemotherapy in the metastatic setting.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Breast Cancer

Authorization of 12 months may be granted for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer when any of the following criteria are met:

A. Verzenio will be used in combination with an aromatase inhibitor as initial endocrine-based therapy.

B. Verzenio will be used in combination with fulvestrant for a member who has experienced disease progression following endocrine therapy.

C. Verzenio will be used as monotherapy for a member who has experienced disease progression following endocrine therapy and prior chemotherapy in the metastatic setting.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES


PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>BRAND NAME* (generic)</th>
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<tr>
<td>VIBERZI (eluxadoline)</td>
<td>Ref# MDC-2 1271-A</td>
</tr>
</tbody>
</table>

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated

FDA-APPROVED INDICATIONS
Viberzi is indicated in adults for the treatment of irritable bowel syndrome with diarrhea (IBS-D).

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has the diagnosis of irritable bowel syndrome with diarrhea (IBS-D)
- AND
- The patient does not have any of the following: A) A history of cholecystectomy, B) A history of chronic or severe constipation or sequelae from constipation, or known or suspected mechanical gastrointestinal obstruction, C) Known or suspected biliary duct obstruction; or sphincter of Oddi disease or dysfunction, D) A history of pancreatitis; or structural diseases of the pancreas, including known or suspected pancreatic duct obstruction, E) Severe hepatic impairment (Child-Pugh Class C), F) Alcoholism, alcohol abuse or alcohol addiction, or a patient who drinks more than 3 alcoholic beverages per day

RATIONALE
These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Viberzi is indicated in adults for the treatment of irritable bowel syndrome with diarrhea (IBS-D).

Viberzi is contraindicated in patients with a history of cholecystectomy, known or suspected biliary duct obstruction or sphincter of Oddi disease or dysfunction, alcoholism, alcohol abuse, or alcohol addiction, or in patients who drink more than 3 alcoholic beverages per day, a history of pancreatitis or structural diseases of the pancreas, including known or suspected pancreatic duct obstruction, severe hepatic impairment (Child-Pugh class C) and a history of chronic or severe constipation or sequelae from constipation, or known or suspected mechanical gastrointestinal obstruction.1-3

REFERENCES
CRITERIA FOR APPROVAL

1. Does the patient have the diagnosis of irritable bowel syndrome with diarrhea (IBS-D)?
   - Yes
   - No

2. Does the patient have any of the following: A) A history of cholecystectomy, B) A history of chronic or severe constipation or sequelae from constipation, or known or suspected mechanical gastrointestinal obstruction, C) Known or suspected biliary duct obstruction; or sphincter of Oddi disease or dysfunction, D) A history of pancreatitis; or structural diseases of the pancreas, including known or suspected pancreatic duct obstruction, E) Severe hepatic impairment (Child-Pugh Class C), F) Alcoholism, alcohol abuse or alcohol addiction, or a patient who drinks more than 3 alcoholic beverages per day?
   - Yes
   - No

Mapping Instructions (1287-A)

<table>
<thead>
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<tbody>
<tr>
<td>1. Go to 2</td>
<td>Deny</td>
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</table>

DENIAL REASONS – DO NOT USE FOR MEDICARE PART D

- You do not meet the requirements of your plan. Your plan covers this drug when you have irritable bowel syndrome with diarrhea.
- Your request has been denied based on the information we have.

[Short Description: No approvable diagnosis]

| 2. Deny | Approve, 36 months |

- You do not meet the requirements of your plan. Your plan covers this drug when you do not have any of these conditions:
  - A history of cholecystectomy (gallbladder removal surgery)
  - A history of chronic or severe constipation or sequelae from constipation, or known or suspected mechanical gastrointestinal obstruction
  - Known or suspected biliary duct obstruction; or sphincter of Oddi disease or dysfunction
  - A history of pancreatitis; or structural diseases of the pancreas, including known or suspected pancreatic duct obstruction
  - Severe hepatic impairment (Child-Pugh Class C)
  - Alcoholism, alcohol abuse or alcohol addiction, or you drink more than 3 alcoholic beverages per day
- Your request has been denied based on the information we have.

[Short Description: Contraindication to therapy]

Guidelines for Approval (MDC-2 1271-A)

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</table>
| 2. Deny | Approve, 12 months | You do not meet the requirements of your plan. Your plan covers this drug when you do not have any of these conditions:
- A history of cholecystectomy (gallbladder removal surgery)
- A history of chronic or severe constipation or sequelae from constipation, or known or suspected mechanical gastrointestinal obstruction
- Known or suspected biliary duct obstruction; or sphincter of Oddi disease or dysfunction
- A history of pancreatitis; or structural diseases of the pancreas, including known or suspected pancreatic duct obstruction
- Severe hepatic impairment (Child-Pugh Class C)
- Alcoholism, alcohol abuse or alcohol addiction, or you drink more than 3 alcoholic beverages per day
Your request has been denied based on the information we have. [Short Description: Contraindication to therapy] |
SPECIALTY GUIDELINE MANAGEMENT

VIEKIRA PAK
VIEKIRA XR
(ombitasvir/paritaprevir/ritonavir/dasabuvir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Viekira Pak/Viekira XR is indicated for the treatment of adult patients with chronic hepatitis C virus (HCV):
A. genotype 1b infection without cirrhosis or with compensated cirrhosis
B. genotype 1a infection without cirrhosis or with compensated cirrhosis for use in combination with ribavirin (RBV)

All other indications are considered experimental/investigational and are not a covered benefit.

II. EXCLUSIONS

Coverage will not be provided for members with decompensated cirrhosis/moderate or severe hepatic impairment (Child Turcotte Pugh Class B or C).

Note: When the requested drug is being used in a combination therapy regimen, exclusions to the other antiviral drugs also apply.

III. CRITERIA FOR APPROVAL

A. Chronic hepatitis C virus infection, in combination with ribavirin
Note: Members with mixed genotype 1 infection or unknown genotype 1 subtype should follow the criteria for approval for genotype 1a infection.

1. Genotype 1a infection
   a. Authorization of up to 12 weeks total may be granted for members without cirrhosis who are either of the following:
      i. Treatment-naïve
      ii. Failed prior treatment with peginterferon alfa (PEG-IFN) and RBV
   b. Authorization of up to 24 weeks total may be granted for members with compensated cirrhosis who are either of the following:
      i. Treatment-naïve
      ii. Failed prior treatment with PEG-IFN and RBV

2. Recurrent HCV infection post liver transplantation
   Authorization of up to 24 weeks total may be granted for members with recurrent HCV infection post liver transplantation who meet all of the following criteria:
a. Genotype 1 infection (irrespective of subtype)
b. Metavir fibrosis score of 2 or lower

**B. Chronic hepatitis C virus infection, without ribavirin**

**Genotype 1b infection**
Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are either of the following:
1. Treatment-naïve
2. Failed prior treatment with PEG-IFN and RBV

**C. HCV and HIV coinfection**
Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in section A or B above are met.

**IV. CONTINUATION OF THERAPY**

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

**V. REFERENCES**

SPECIALTY GUIDELINE MANAGEMENT

SABRIL (vigabatrin) tablets and powder for oral solution
vigabatrin powder for oral solution

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Infantile spasms: Sabril is indicated as monotherapy for pediatric patients with infantile spasms one month to two years of age for whom the potential benefits outweigh the potential risk of vision loss.

2. Complex Partial Seizures: Sabril is indicated as adjunctive therapy for adults and pediatric patients ten years of age and older with refractory complex partial seizures who have inadequately responded to several alternative treatments and for whom the potential benefits outweigh the risk of vision loss. Sabril is not indicated as a first line agent for complex partial seizures.

B. Compendial Use: Refractory complex partial seizures in children younger than ten years of age who have inadequately responded to at least two alternative treatments.

All other indications are considered experimental/investigational and are not covered benefits.

II. CRITERIA FOR INITIAL APPROVAL

A. Infantile Spasms

Authorization of 4 weeks may be granted for treatment of infantile spasms.

B. Complex Partial Seizures

Authorization of 3 months may be granted for treatment of complex partial seizures when member has had an inadequate response to at least two alternative treatments for complex partial seizures.

III. CONTINUATION OF THERAPY

A. Infantile Spasms

Authorization of 6 months may be granted for members requesting Sabril for continuation of therapy when member has shown substantial clinical benefit from Sabril therapy.

B. Complex Partial Seizures

Authorization of 12 months may be granted for members requesting Sabril for continuation of therapy when member has shown substantial clinical benefit from Sabril therapy.
IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

VIMIZIM (elosulfase alfa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Vimizim is indicated for patients with Mucopolysaccharidosis type IVA (MPS IVA, Morquio A syndrome).

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Mucopolysaccharidosis IVA (MPS IVA)
Indefinite authorization may be granted for treatment of MPS IVA when the diagnosis of MPS IVA was confirmed by enzyme assay demonstrating a deficiency of N-acetylgalactosamine 6-sulfatase enzyme activity or by genetic testing.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

VITRAKVI (larotrectinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Vitrakvi is indicated for the treatment of adult and pediatric patients with solid tumors that:
• have a neurotrophic receptor tyrosine kinase (NTRK) gene fusion without a known acquired resistance mutation,
• are metastatic or where surgical resection is likely to result in severe morbidity, and
• have no satisfactory alternative treatments or that have progressed following treatment.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Solid tumors with a NTRK gene fusion
Authorization of 12 months may be granted for treatment of solid tumors when all of the following criteria are met:
A. The tumors have a NTRK gene fusion without a known acquired resistance mutation, as demonstrated by laboratory testing (e.g., next-generation sequencing [NGS] or fluorescence in situ hybridization [FISH]).
B. The disease is metastatic or surgical resection is likely to result in severe morbidity.
C. No satisfactory alternative treatments are available or disease has progressed following standard systemic treatment for the disease.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

VIVITROL (naltrexone for extended-release injectable suspension)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
A. Vivitrol is indicated for the treatment of alcohol dependence in patients who are able to abstain from alcohol in an outpatient setting prior to initiation of treatment with Vivitrol. Patients should not be actively drinking at the time of initial Vivitrol administration.
B. Vivitrol is indicated for the prevention of relapse to opioid dependence, following opioid detoxification.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Alcohol Dependence
   Authorization of 24 months may be granted for treatment of alcohol dependence.

B. Opioid Dependence
   Authorization of 24 months may be granted for prevention of relapse to opioid dependence.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

VIZIMPRO (dacomitinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Vizimpro is indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletion or exon 21 L858R substitution mutations as detected by an FDA-approved test.

All other indications are considered experimental/investigational and are not a covered benefit.

Compendial Uses

NSCLC, recurrent, advanced or metastatic sensitizing EGFR mutation-positive

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: For NSCLC, EGFR mutation testing results.

III. CRITERIA FOR INITIAL APPROVAL

Non-small cell lung cancer (NSCLC)

Authorization of 12 months may be granted for treatment of recurrent, advanced or metastatic NSCLC when the member has sensitizing EGFR mutation-positive disease.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced an unacceptable toxicity.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

VONVENDI [von Willebrand factor (recombinant)]

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Vonvendi is indicated for use in adults (age 18 and older) diagnosed with von Willebrand disease (VWD) for:
1. On-demand treatment and control of bleeding episodes
2. Perioperative management of bleeding

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Von Willebrand Disease
Indefinite authorization may be granted for treatment of vWD when any of the following criteria is met:
A. Member has type 1, 2A, 2M, or 2N vWD and has had an insufficient response to desmopressin or a documented clinical reason for not using desmopressin (see Appendix).
B. Member has type 2B or type 3 vWD.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. APPENDIX

Clinical Reasons For Not Utilizing Desmopressin in Patients with Type 1, 2A, 2N and 2M vWD
A. Age < 2 years
B. Pregnancy
C. Fluid/electrolyte imbalance
D. High risk for cardiovascular or cerebrovascular disease (especially the elderly)
E. Predisposition to thrombus formation
F. Trauma requiring surgery
G. Life-threatening bleed
H. Contraindication or intolerance to desmopressin
I. Severe type 1 von Willebrand disease
V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

VOSEVI (sofosbuvir/velpatasvir/voxilaprevir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Vosevi is indicated for the treatment of adult patients with chronic hepatitis C virus (HCV) infection without cirrhosis or with compensated cirrhosis (Child-Pugh A) who have:

- Genotype 1, 2, 3, 4, 5, or 6 infection and have previously been treated with an HCV regimen containing an NS5A inhibitor
- Genotype 1a or 3 infection and have previously been treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor

Additional benefit of Vosevi over sofosbuvir/velpatasvir was not shown in adults with genotype 1b, 2, 4, 5, or 6 infection previously treated with sofosbuvir without an NS5A inhibitor.

All other indications are considered experimental/investigational and are not a covered benefit.

II. EXCLUSIONS

Coverage will not be provided for members with decompensated cirrhosis/moderate or severe hepatic impairment (Child Turcotte Pugh Class B or C)

Note: When the requested drug is being used in a combination therapy regimen, exclusions to the other antiviral drugs also apply.

III. CRITERIA FOR INITIAL APPROVAL

A. Chronic hepatitis C virus infection, without ribavirin

1. Genotype 1a infection
   a. Authorization of up to 12 weeks total may be granted for members who failed prior treatment with a sofosbuvir-containing regimen without an HCV NS5A inhibitor.
   b. Authorization of up to 12 weeks total may be granted for members who failed prior treatment with an HCV NS5A inhibitor-containing regimen.

2. Genotype 1b infection
   Authorization of up to 12 weeks total may be granted for members who failed prior treatment with an HCV NS5A inhibitor-containing regimen.

3. Genotype 2 infection
Authorization of up to 12 weeks total may be granted for members who failed prior treatment with an HCV NS5A inhibitor-containing regimen.

4. **Genotype 3 infection**
   a. Authorization of up to 12 weeks total may be granted for members who failed prior treatment with any direct-acting antiviral regimen (eg, NS5A- or sofosbuvir-containing regimen).
   b. Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who are treatment naive and have the Y93H substitution associated with velpatasvir resistance.
   c. Authorization of up to 12 weeks total may be granted for members who failed prior treatment with PEG-IFN and RBV and meet one of the following:
      i. Member does not have cirrhosis and has the Y93H substitution associated with velpatasvir resistance.
      ii. Member has compensated cirrhosis.

5. **Genotype 4, 5, or 6 infection**
   Authorization of up to 12 weeks total may be granted for members who failed prior treatment with any direct-acting antiviral regimen (eg, NS5A- or sofosbuvir-containing regimen).

B. **Chronic hepatitis C virus infection, in combination with ribavirin**

   **Genotype 3 infection**
   Authorization of up to 12 weeks total may be granted for members with cirrhosis who failed prior treatment with an HCV NS5A inhibitor-containing regimen.

C. **HCV and HIV Coinfection**
   Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A or B above are met.

IV. **CONTINUATION OF THERAPY**

   All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. **REFERENCES**

SPECIALTY GUIDELINE MANAGEMENT

VOTRIENT (pazopanib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Advanced renal cell carcinoma (RCC)
   2. Advanced soft tissue sarcoma (STS) in patients who have received prior chemotherapy

   Limitations of Use: The efficacy of Votrient for the treatment of patients with adipocytic STS or gastrointestinal stromal tumors has not been demonstrated.

B. Compendial Uses
   1. Relapsed or surgically unresectable stage IV RCC
   2. Uterine sarcoma
   3. Soft tissue sarcoma that is not an adipocytic sarcoma
   4. Thyroid carcinoma (medullary, papillary, Hürthle cell, or follicular)
   5. Bone cancer of one of the following subtypes:
      a. Chordoma
      b. Chondrosarcoma
      c. Osteosarcoma

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Renal Cell Carcinoma
   Authorization of 12 months may be granted for treatment of relapsed, metastatic, or unresectable renal cell carcinoma.

B. Soft Tissue Sarcoma (STS)
   Authorization of 12 months may be granted for treatment of soft tissue sarcoma (STS) that is not an adipocytic sarcoma.

C. Uterine Sarcoma
   Authorization of 12 months may be granted for treatment of recurrent or metastatic uterine sarcoma.

D. Thyroid Carcinoma
   Authorization of 12 months may be granted for treatment of radioiodine refractory papillary, Hürthle cell, or follicular thyroid carcinoma.
E. Medullary Thyroid Carcinoma  
Authorization of 12 months may be granted for the treatment of medullary thyroid carcinoma when either of the following criteria are met:
1. Member has an intolerance or contraindication to cabozantinib and vandetanib.
2. Member has disease progression on cabozantinib or vandetanib.

F. Bone cancer  
Authorization of 12 months may be granted for treatment of one of the following subtypes of bone cancer:
1. Chordoma
2. Chondrosarcoma
3. Osteosarcoma

III. CONTINUATION OF THERAPY  
Authorization of 12 months may be granted for continuation of therapy for an indication outlined in Section II when there is no evidence of unacceptable toxicity or disease progression on the current regimen.

IV. REFERENCES  
SPECIALTY GUIDELINE MANAGEMENT

VPRIV (velaglucose alfa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

VPRIV is indicated for long-term enzyme replacement therapy (ERT) for patients with type 1 Gaucher disease.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Gaucher disease type 1

Indefinite authorization may be granted for treatment of Gaucher disease type 1 when the diagnosis of Gaucher disease was confirmed by enzyme assay demonstrating a deficiency of beta-glucocerebrosidase (glucosidase) enzyme activity or by genetic testing.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

VYNDAXEL (tafamidis meglumine)  
VYNDAMAX (tafamidis)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Vyndaqel and Vyndamax are transthyretin stabilizers indicated for the treatment of the cardiomyopathy of wild type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) in adults to reduce cardiovascular mortality and cardiovascular-related hospitalization.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Biopsy results or technetium-labeled bone scintigraphy tracing results confirming presence of amyloid deposits
B. Echocardiography or cardiac magnetic resonance imaging results confirming cardiac involvement
C. For members with hereditary ATTR-CM: results confirming a mutation of the transthyretin (TTR) gene
D. For members with wild type ATTR-CM: immunohistochemical analysis, scintigraphy, or mass spectrometry results confirming transthyretin precursor proteins
E. For continuation of therapy: Medical record documentation confirming the member demonstrates a beneficial response to treatment (e.g., improvement in rate of disease progression as demonstrated by distance walked on the 6-minute walk test, the Kansas City Cardiomyopathy Questionnaire—Overall Summary (KCCQ-OS) score, cardiovascular-related hospitalizations, NYHA classification of heart failure, left ventricular stroke volume, NT-proBNP level)

III. CRITERIA FOR INITIAL APPROVAL

Cardiomyopathy of Wild Type or Hereditary Transthyretin-mediated Amyloidosis

Authorization of 12 months may be granted for treatment of cardiomyopathy of wild type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) when all of the following criteria are met:
A. The diagnosis is confirmed by presence of amyloid deposits on analysis of biopsy from cardiac or noncardiac sites (e.g., fat aspirate, gastrointestinal sites, salivary glands, bone marrow) or by technetium-labeled bone scintigraphy tracing
B. Cardiac involvement was confirmed by echocardiography or cardiac magnetic resonance imaging (e.g., end-diastolic interventricular septal wall thickness exceeding 12 mm)
C. For members with hereditary ATTR-CM, presence of a mutation of the TTR gene was confirmed.
D. For members with wild type ATTR-CM, presence of transthyretin precursor proteins was confirmed by immunohistochemical analysis, scintigraphy, or mass spectrometry.
E. The member exhibits clinical symptoms of cardiomyopathy and heart failure (e.g., dyspnea, fatigue, orthostatic hypotension, syncope, peripheral edema).
F. The member is not a liver transplant recipient.
G. The requested medication will not be used in combination with inotersen (Tegsedi) or patisiran (Onpattro).

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for the continued treatment of ATTR-CM when all of the following criteria are met:
A. The member must have met all initial authorization criteria.
B. The member must have demonstrated a beneficial response to treatment with tafamidis therapy [e.g., improvement in rate of disease progression as demonstrated by distance walked on the 6-minute walk test, the Kansas City Cardiomyopathy Questionnaire–Overall Summary (KCCQ-OS) score, cardiovascular-related hospitalizations, NYHA classification of heart failure, left ventricular stroke volume, N-terminal B-type natriuretic peptide (NT-proBNP) level]. Documentation from the medical record must be provided.

REFERENCES

## PRIOR AUTHORIZATION CRITERIA

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**Status:** CVS Caremark Criteria  
**Type:** Initial Prior Authorization with Quantity Limit  
**Ref # 3176-C**

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

### FDA-APPROVED INDICATIONS
Wakix is indicated for the treatment of excessive daytime sleepiness (EDS) in adult patients with narcolepsy.

### COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has narcolepsy confirmed by sleep lab evaluation
- The patient has experienced an inadequate treatment response to a central nervous system (CNS) stimulant (e.g., amphetamine, dextroamphetamine, methylphenidate)
- The patient has experienced an intolerance to a central nervous system (CNS) stimulant (e.g., amphetamine, dextroamphetamine, methylphenidate)
- The patient has a contraindication that would prohibit a trial of central nervous system (CNS) stimulants (e.g., amphetamine, dextroamphetamine, methylphenidate)
- The patient has experienced an inadequate treatment response to armodafinil OR modafinil
- The patient has experienced an intolerance to armodafinil OR modafinil
- The patient has a contraindication that would prohibit a trial of ALL of the following: A) armodafinil, B) modafinil

Quantity Limits Apply.

### RATIONALE
The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Wakix is indicated for the treatment of excessive daytime sleepiness (EDS) in adult patients with narcolepsy.

According to the American Academy of Sleep Medicine (AASM), successful treatment of hypersomnia of central origin requires an accurate diagnosis, individual tailoring of therapy to produce the fullest possible return of normal function, and regular follow-up to monitor response to treatment. The evaluation should include a thorough evaluation of other possible contributing causes of excessive daytime sleepiness. The International Classification of Sleep Disorders, Third Edition (ICSD-3) specifies necessary diagnostic tests and criteria for each disorder of central origin. For narcolepsy, a sleep lab evaluation consisting of an overnight polysomnography (PSG) and mean sleep latency tests (MSLT) is recommended to
confirm the diagnosis. Many other conditions produce such sleepiness and can mimic or coexist with a hypersomnia of central origin.4

According to AASM guidelines, modafinil is effective for the treatment of daytime sleepiness due to narcolepsy. One additional study of 196 subjects involved assessment of armodafinil (the longer half-life enantiomer of modafinil) for treatment of excessive sleepiness in patients with narcolepsy.4 Subjects receiving armodafinil experienced significant improvement in sleepiness as measured by the Mean Wakefulness Test (MWT) mean sleep latency, and in the Clinical Global Impression of Change.4 The guidelines also state that amphetamine, dextroamphetamine, and methylphenidate are effective for treatment of daytime sleepiness due to narcolepsy.4 Therefore, patients who have an inadequate treatment response, intolerance, or contraindication to a CNS stimulant and either modafinil or armodafinil will be considered for approval.

The recommended dosage range of Wakix in patients with narcolepsy is 17.8 mg to 35.6 mg once daily. Dosage should be titrated, starting with 8.9 mg once daily and increasing to 17.8 mg after one week of therapy. After one week of therapy at 17.8 mg once daily, dosage may be increased to the maximum recommended dosage of 35.6 mg once daily. Patients with moderate hepatic impairment and renal impairment should initiate Wakix at 8.9 mg once daily and increase to a maximum recommended dose of 17.8 mg once daily. Wakix is available as 4.45 mg tablets and 17.8 mg tablets. Approvals will have a limit of 60 tablets per month to allow for the initial starting dose and then up to the maximum recommended daily dose of 35.6 mg.

REFERENCES


CRITERIA FOR APPROVAL

1. Does the patient have a diagnosis of narcolepsy confirmed by sleep lab evaluation? Yes No

2. Has the patient experienced an inadequate treatment response to a central nervous system (CNS) stimulant (e.g., amphetamine, dextroamphetamine, methylphenidate)? [If yes, then skip to question 5.] Yes No

3. Has the patient experienced an intolerance to a central nervous system (CNS) stimulant (e.g., amphetamine, dextroamphetamine, methylphenidate)? [If yes, then skip to question 5.] Yes No

4. Does the patient have a contraindication that would prohibit a trial of central nervous system (CNS) stimulants (e.g., amphetamine, dextroamphetamine, methylphenidate)? Yes No
5. Has the patient experienced an inadequate treatment response to armodafinil OR modafinil?  
   [If yes, then skip to question 8.]

6. Has the patient experienced an intolerance to armodafinil OR modafinil?  
   [If yes, then skip to question 8.]

7. Does the patient have a contraindication to that would prohibit a trial of ALL of the following: A) armodafinil, B) modafinil?  

8. Does the patient require MORE than the plan allowance of 60 tablets per month?  
   [RPh Note: If yes, then deny and enter a partial approval for 60 tablets/25 days or 180 tablets/75 days.]

Mapping Instructions

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
<th>DENIAL REASONS – DO NOT USE FOR MEDICARE PART D</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Go to 2</td>
<td>Deny</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have narcolepsy confirmed by sleep lab testing. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]</td>
</tr>
<tr>
<td>2.</td>
<td>Go to 5</td>
<td>Go to 3</td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>Go to 5</td>
<td>Go to 4</td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>Go to 5</td>
<td>Deny</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have tried a central nervous system (CNS) stimulant drug (e.g., amphetamine, dextroamphetamine, or methylphenidate) and it either did not work for you, or you cannot use it. Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance, or contraindication to a CNS stimulant drug]</td>
</tr>
<tr>
<td>5.</td>
<td>Go to 8</td>
<td>Go to 6</td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>Go to 8</td>
<td>Go to 7</td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>Go to 8</td>
<td>Deny</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when you have tried armodafinil or modafinil and it did not work for you, or you cannot use it. Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance, or contraindication to armodafinil or modafinil]</td>
</tr>
<tr>
<td>8.</td>
<td>Deny</td>
<td>Approve, 12 months, 60 tablets/25 days* or 180 tablets/75 days*</td>
<td>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 60 tablets/month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]</td>
</tr>
</tbody>
</table>

*The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.
SPECIALTY GUIDELINE MANAGEMENT

WILATE (von Willebrand factor/coagulation factor VIII complex [human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. **FDA-Approved Indication**
   Wilate is indicated in children and adults with von Willebrand Disease (vWD) for:
   1. On-demand treatment and control of bleeding episodes
   2. Perioperative management of bleeding

B. **Compendial Use**
   Acquired von Willebrand Syndrome

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. **Von Willebrand Disease**
   Indefinite authorization may be granted for treatment of vWD when either of the following criteria is met:
   1. Member has type 1, 2A, 2M, or 2N vWD and has had an insufficient response to desmopressin or a documented clinical reason for not using desmopressin (see Appendix).
   2. Member has type 2B or type 3 vWD.

B. **Acquired von Willebrand Syndrome**
   Indefinite authorization may be granted for treatment of acquired von Willebrand syndrome.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. APPENDIX

**Clinical Reasons For Not Utilizing Desmopressin in Patients with Type 1, 2A, 2N and 2M vWD**

A. Age < 2 years
B. Pregnancy
C. Fluid/electrolyte imbalance
D. High risk for cardiovascular or cerebrovascular disease (especially the elderly)
E. Predisposition to thrombus formation
F. Trauma requiring surgery
G. Life-threatening bleed
H. Contraindication or intolerance to desmopressin
I. Severe type 1 von Willebrand disease

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

XALKORI (crizotinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Xalkori is indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK) or ROS1-positive as detected by an FDA-approved test.

B. Compendial Uses

1. NSCLC, recurrent, advanced or metastatic ALK rearrangement-positive or ROS1 rearrangement-positive tumors
2. NSCLC with high-level MET amplification or MET exon 14 skipping mutation
3. Inflammatory myofibroblastic tumor (IMT) with ALK translocation
4. Anaplastic large cell lymphoma, relapsed or refractory ALK-positive
5. Recurrent brain metastases from ALK rearrangement-positive NSCLC or ROS1 rearrangement-positive NSCLC

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: ALK mutation or translocation status, ROS-1 mutation status, MET exon 14 skipping mutation status, or high-level MET amplification status (where applicable).

III. CRITERIA FOR INITIAL APPROVAL

A. Non-small cell lung cancer (NSCLC)

Authorization of 12 months may be granted for treatment of NSCLC when the member meets any of the following criteria:
1. Member has recurrent, advanced or metastatic ALK-positive NSCLC (including brain metastases from NSCLC).
2. Member has recurrent, advanced or metastatic ROS1-positive NSCLC (including brain metastases from NSCLC).
3. Member has NSCLC with high-level MET amplification or MET exon 14 skipping mutation.

B. Inflammatory myofibroblastic tumor (IMT)

Authorization of 12 months may be granted for treatment of ALK-positive IMT.
C. Anaplastic large cell lymphoma (ALCL)
Authorization of 12 months may be granted for treatment of relapsed or refractory ALK-positive ALCL.

IV. CONTINUATION OF THERAPY
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication in Section III who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

XELJANZ (tofacitinib)
XELJANZ XR (tofacitinib extended release tablets)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
A. Moderately to severely active rheumatoid arthritis
B. Active psoriatic arthritis
C. Moderately to severely active ulcerative colitis

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active rheumatoid arthritis (RA)
   1. Authorization of 24 months may be granted to members who have previously received tofacitinib or any biologic DMARD indicated for the treatment of moderately to severely active rheumatoid arthritis.

   2. Authorization of 24 months may be granted for treatment of moderately to severely active RA when any of the following criteria is met:
   i. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
   ii. Member has an intolerance or contraindication to methotrexate (see Appendix).

B. Active psoriatic arthritis (PsA)
   1. Authorization of 24 months may be granted to members who have previously received tofacitinib or any biologic DMARD indicated for the treatment of active psoriatic arthritis. Tofacitinib must be used in combination with a nonbiologic DMARD (e.g., methotrexate, leflunomide, sulfasalazine, etc.)

   2. Authorization of 24 months may be granted for treatment of active PsA when all of the following criteria are met:
   i. Member has experienced an inadequate response to at least a 3-month trial of methotrexate (MTX) or other nonbiologic disease-modifying antirheumatic drugs (DMARDs) (e.g., leflunomide, sulfasalazine, etc.)
   ii. Tofacitinib is used in combination with a nonbiologic DMARD (e.g., methotrexate, leflunomide, sulfasalazine, etc.)

C. Moderately to severely active ulcerative colitis (UC)
   1. Authorization of 24 months may be granted for members who have previously received tofacitinib for the treatment of moderately to severely active ulcerative colitis.
2. Authorization of 24 months may be granted for treatment of moderately to severely active UC if the member has had an inadequate response or intolerance to at least one tumor necrosis factor (TNF) inhibitor.

III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with tofacitinib as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB).

Note: Members who have received tofacitinib or any other biologic DMARD are exempt from requirements related to TB screening in this Policy.

V. APPENDIX

Examples of Contraindications to Methotrexate
1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy
10. Renal impairment
11. Significant drug interaction

VI. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

XELODA (capecitabine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Colorectal Cancer
   a. Xeloda is indicated as a single agent for adjuvant treatment in patients with Dukes' C colon cancer who have undergone complete resection of the primary tumor when treatment with fluoropyrimidine therapy alone is preferred.
   b. Xeloda is indicated as first-line treatment in patients with metastatic colorectal carcinoma when treatment with fluoropyrimidine therapy alone is preferred.

2. Breast Cancer
   a. Xeloda in combination with docetaxel is indicated for the treatment of patients with metastatic breast cancer after failure of prior anthracycline-containing chemotherapy.
   b. Xeloda monotherapy is also indicated for the treatment of patients with metastatic breast cancer resistant to both paclitaxel and an anthracycline-containing chemotherapy regimen or resistant to paclitaxel and for whom further anthracycline therapy is not indicated, for example, patients who have received cumulative doses of 400 mg/m² of doxorubicin or doxorubicin equivalents.

B. Compendial Uses

1. Anal cancer
2. Breast cancer
3. Central nervous system (CNS) metastases from breast cancer
4. Colorectal Cancer
5. Esophageal and esophagogastric junction cancer
6. Gastric cancer
7. Head and neck cancer
8. Hepatobiliary cancers (extra-/intra-hepatic cholangiocarcinoma and gallbladder cancer)
9. Occult primary tumors (cancer of unknown primary)
10. Ovarian cancer (Epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer/mucinous cancer)
11. Pancreatic adenocarcinoma
12. Penile cancer
13. Neuroendocrine and adrenal tumors

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Colorectal Cancer (CRC)

Authorization of 12 months may be granted for the treatment of colorectal cancer.
B. Breast Cancer
Authorization of 12 months may be granted for the treatment of recurrent or metastatic breast cancer.

C. Neuroendocrine and Adrenal Tumors
Authorization of 12 months may be granted for the treatment of neuroendocrine and adrenal tumors.

D. Pancreatic Adenocarcinoma
Authorization of 12 months may be granted for the treatment of pancreatic adenocarcinoma.

E. Esophageal and Esophagogastric Junction Cancers
Authorization of 12 months may be granted for the treatment of esophageal and esophagogastric junction cancers.

F. Gastric Cancer
Authorization of 12 months may be granted for the treatment of gastric cancer.

G. Extrahepatic and Intrahepatic Cholangiocarcinoma and Gallbladder Cancer
Authorization of 12 months may be granted for the treatment of extrahepatic and intrahepatic cholangiocarcinoma and gallbladder cancer.

H. Ovarian Cancer
Authorization of 12 months may be granted for the treatment of ANY of the following:
1. Epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer
2. Mucinous carcinoma

I. Head and Neck Cancer
Authorization of 12 months may be granted for the treatment of head and neck cancer.

J. CNS Metastases from Breast Cancer
Authorization of 12 months may be granted for the treatment of CNS metastases from breast cancer.

K. Occult Primary Tumors (cancer of unknown primary)
Authorization of 12 months may be granted for the treatment of occult primary tumors.

L. Penile Cancer
Authorization of 12 months may be granted for the treatment of penile cancer.

M. Anal Cancer
Authorization of 12 months may be granted for the treatment of anal cancer.

III. CONTINUATION OF THERAPY
All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria.

IV. REFERENCES
PRIOR AUTHORIZATION CRITERIA

**BRAND NAME***
(generic)

XENLETA
(lefamulin)

*Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

**FEMA-APPROVED INDICATIONS**
Xenleta is indicated for the treatment of adults with community-acquired bacterial pneumonia (CABP) caused by the following susceptible microorganisms: Streptococcus pneumoniae, Staphylococcus aureus (methicillin-susceptible isolates), Haemophilus influenzae, Legionella pneumophila, Mycoplasma pneumoniae, and Chlamydophila pneumoniae.

**COVERAGE CRITERIA**
The requested drug will be covered with prior authorization when the following criteria are met:

- The patient is being converted from intravenous (IV) lefamulin (Xenleta) as prescribed or directed by an Infectious Disease specialist

OR

- The requested drug is being prescribed for community-acquired bacterial pneumonia (CABP) caused by any of the following susceptible microorganisms: A) Streptococcus pneumoniae, B) Staphylococcus aureus (methicillin-susceptible isolates), C) Haemophilus influenzae, D) Legionella pneumophila, E) Mycoplasma pneumoniae, F) Chlamydophila pneumoniae.

AND

- The infection is proven or strongly suspected to be caused by susceptible bacteria

AND

- The patient has experienced an inadequate treatment response, intolerance, or contraindication to alternative therapies OR the bacteria are NOT susceptible to any other antibiotics

**RATIONALE**
The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Xenleta is indicated for the treatment of adults with community-acquired bacterial pneumonia (CABP) caused by the following susceptible microorganisms: Streptococcus pneumoniae, Staphylococcus aureus (methicillin-susceptible isolates), Haemophilus influenzae, Legionella pneumophila, Mycoplasma pneumoniae, and Chlamydophila pneumoniae.

Xenleta (lefamulin) will be approved if being requested for a patient converted from intravenous (IV) Xenleta as prescribed or directed by an Infectious Disease specialist.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Xenleta and other antibacterial drugs, Xenleta should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy. To limit potential for widespread resistance, clinicians should consider reserving lefamulin for use in more severe infections in consultation with an infectious disease specialist. Choices should be modified on the basis of susceptibility test results and advice from specialists.

For treatment of adults with CABP, the recommended dosage of Xenleta is 150 mg every 12 hours by intravenous infusion over 60 minutes for 5 to 7 days and 600 mg orally every 12 hours for 5 days. Therefore, to allow for max recommended duration of therapy, the approval will be for 7 days.
REFERENCES
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA.

Written by: ME
Date Written: 08/2019
Revised: (CHART) 9/05/19
Reviewed: External Review: 10/2019

CRITERIA FOR APPROVAL

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Is the patient being converted from intravenous (IV) lefamulin (Xenleta) as prescribed or directed by an Infectious Disease specialist? [If yes, then no further questions.] Yes No</td>
<td></td>
</tr>
<tr>
<td>2. Is the requested drug being prescribed for community-acquired bacterial pneumonia (CABP) caused by any of the following susceptible microorganisms: A) Streptococcus pneumoniae, B) Staphylococcus aureus (methicillin-susceptible isolates), C) Haemophilus influenzae, D) Legionella pneumophila, E) Mycoplasma pneumoniae, F) Chlamydophila pneumoniae? Yes No</td>
<td></td>
</tr>
<tr>
<td>3. Is the infection proven or strongly suspected to be caused by susceptible bacteria? Yes No</td>
<td></td>
</tr>
<tr>
<td>4. Has the patient experienced an inadequate treatment response, intolerance, or contraindication to alternative therapies OR are the bacteria NOT susceptible to any other antibiotics? Yes No</td>
<td></td>
</tr>
</tbody>
</table>

Mapping Instructions

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
<th>DENIAL REASONS – DO NOT USE FOR MEDICARE PART D</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Approve, 7 days</td>
<td>Go to 2</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when all of these conditions apply: - You have pneumonia that is caused by a specific bacteria - The specific bacteria are susceptible to the drug Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]</td>
</tr>
<tr>
<td>2. Go to 3</td>
<td>Deny</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when all of these conditions apply: - Tests show or strongly suggest you have an infection - The pneumonia is caused by a specific bacteria - The specific bacteria are susceptible to the drug Your request has been denied based on the information we have.</td>
</tr>
<tr>
<td>3. Go to 4</td>
<td>Deny</td>
<td>You do not meet the requirements of your plan. Your plan covers this drug when all of these conditions apply: - Tests show or strongly suggest you have an infection - The pneumonia is caused by a specific bacteria - The specific bacteria are susceptible to the drug Your request has been denied based on the information we have.</td>
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</tr>
<tr>
<td>4.</td>
<td>Approve, 7 days</td>
<td>Deny</td>
</tr>
</tbody>
</table>

You do not meet the requirements of your plan.
Your plan covers this drug when you meet one of these conditions:
- You have tried other drugs and they either did not work for you or you cannot use them
- The specific bacteria are not susceptible to any other drugs
Your request has been denied based on the information we have.

[Short Description: No approvable diagnosis]
SPECIALTY GUIDELINE MANAGEMENT

XEOMIN (incobotulinumtoxinA)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
A. Cervical dystonia in adult patients
B. Blepharospasm in adults
C. Upper limb spasticity in adults
D. Chronic sialorrhea in adults

All other indications are considered experimental/investigational and are not a covered benefit.

II. EXCLUSIONS

Coverage will not be provided for cosmetic use.

III. CRITERIA FOR INITIAL APPROVAL

A. Cervical dystonia
   Authorization of 24 months may be granted for treatment of cervical dystonia (e.g., torticollis).

B. Blepharospasm
   Authorization of 24 months may be granted for treatment of blepharospasm.

C. Upper limb spasticity
   Authorization of 24 months may be granted for treatment of upper limb spasticity.

D. Chronic sialorrhea
   Authorization of 24 months may be granted for treatment of chronic sialorrhea.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

XERMELO (telotristat ethyl)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Xermelo is indicated for the treatment of carcinoid syndrome diarrhea in combination with somatostatin analog (SSA) therapy in adults inadequately controlled by SSA therapy.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Carcinoid syndrome diarrhea
Authorization of 12 months may be granted for the treatment of carcinoid syndrome diarrhea when all of the following criteria are met:
A. Member has had an inadequate response to somatostatin analog (SSA) therapy.
B. Xermelo will be used in combination with SSA therapy.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

XGEVA (denosumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Prevention of skeletal-related events in patients with multiple myeloma and in patients with bone metastases from solid tumors
   2. Treatment of adults and skeletally mature adolescents with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity
   3. Treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy

B. Compendial Uses
   Second line therapy for osteopenia or osteoporosis in patients with systemic mastocytosis

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Multiple myeloma
   Authorization of 12 months may be granted for the prevention of skeletal-related events in members with multiple myeloma.

B. Bone Metastases from a Solid Tumor
   Authorization of 12 months may be granted for the treatment of bone metastases from a solid tumor.

C. Giant cell tumor of bone
   Authorization of 12 months may be granted for the treatment of giant cell tumor of bone.

D. Hypercalcemia of malignancy
   Initial authorization of 2 months may be granted for the treatment of hypercalcemia of malignancy that is refractory to intravenous (IV) bisphosphonate therapy OR there is a clinical reason to avoid IV bisphosphonate therapy (See Appendix).

E. Systemic mastocytosis
   Authorization of 12 months may be granted for second-line therapy for osteopenia or osteoporosis in members with systemic mastocytosis that have not responded to therapy with bisphosphonates or for patients who are not candidates for bisphosphonates because of renal insufficiency.
III. CONTINUATION OF THERAPY

A. Hypercalcemia of malignancy
   Authorization of 2 months will be granted for continued treatment in members requesting reauthorization for hypercalcemia of malignancy who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

B. All Diagnosis (excluding hypercalcemia of malignancy)
   Authorization of 12 months will be granted for continued treatment in members requesting reauthorization for an indication listed in Section II (excluding hypercalcemia of malignancy) who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. APPENDIX

   Clinical reasons to avoid IV bisphosphonate therapy
   • Renal insufficiency (creatinine clearance <35 mL/min)
   • Acute renal impairment
   • History of intolerance to an IV bisphosphonate
   • Hypocalcemia

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

XIAFLEX (collagenase clostridium histolyticum)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
1. Xiaflex is indicated for the treatment of adult patients with Dupuytren’s contracture with a palpable cord.
2. Xiaflex is indicated for the treatment of adult men with Peyronie’s disease with a palpable plaque and curvature deformity of at least 30 degrees at the start of therapy.

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Dupuytren’s contracture: Chart notes or medical record indicating the affected joint, contracture, and a positive table top test (for new starts and continuation) and the number of injections the member has received (for continuation only).
B. Peyronie’s disease: Chart notes or medical record indicating palpable plaque, curvature, intact erectile function (for new starts and continuation) and the number of injections the member has received (for continuation only).

III. CRITERIA FOR INITIAL APPROVAL

A. Dupuytren’s contracture
Authorization of 6 months may be granted for the treatment of Dupuytren’s contracture when all of the following criteria are met:
1. The member has a finger flexion contracture with a palpable cord in a metacarpophalangeal joint or a proximal interphalangeal joint prior to initiating Xiaflex therapy.
2. The contracture is at least 20 degrees prior to initiating Xiaflex therapy.
3. The member had a positive table top test, defined as the inability to simultaneously place the affected finger(s) and palm flat against a table prior to initiating Xiaflex therapy.
4. The member will receive a maximum of 3 injections per cord (4 weeks apart) as part of the current treatment.

B. Peyronie’s disease
Authorization of 12 months may be granted for the treatment of Peyronie’s disease when the following criteria are met:
1. The member has stable Peyronie’s disease without clinical changes (e.g., worsening curvature) for at least three months.
2. The member has a palpable plaque and curvature deformity of at least 30 degrees and less than 90 degrees prior to initiating Xiaflex therapy.
3. The member has intact erectile function (with or without medication).
4. The member is 18 years of age or older.
5. The member will receive a maximum of one treatment course with a maximum of 8 injections total, including any injections the patient has received for any previous treatment.

IV. CONTINUATION OF THERAPY

A. **Dupuytren’s contracture**
   Authorization of 6 months may be granted for the continuation of treatment for Dupuytren’s contracture when all of the following criteria are met:
   1. The patient meets all initial authorization criteria.
   2. The member is continuing with a treatment course for the same cord. For treatment of a new cord or a previously-treated cord following recurrence, member must meet all initial authorization criteria.
   3. The member has received less than 3 injections total per cord (4 weeks apart).

B. **Peyronie’s disease**
   Authorization of 12 months may be granted for the continuation of treatment for Peyronie’s disease when all of the following criteria are met:
   1. The member meets all initial authorization criteria.
   2. The member has curvature deformity of at least 15 degrees at the time of the continuation request.
   3. The member has received less than 8 injections total, including any injections the patient has received for any previous treatment.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

XOLAIR (omalizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Allergic asthma

Xolair is indicated for patients 6 years of age and older with moderate to severe persistent asthma who have a positive skin test or in vitro reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids.

Limitations of use: Xolair is not indicated for the relief of acute bronchospasm or status asthmaticus, or for treatment of other allergic conditions.

B. Chronic idiopathic urticaria (CIU)

Xolair is indicated for the treatment of adults and adolescents 12 years of age and older with chronic idiopathic urticaria (CIU) who remain symptomatic despite H1 antihistamine treatment.

Limitations of use: Xolair is not indicated for treatment of other forms of urticaria.

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Asthma: Member’s chart or medical record showing pre-treatment IgE level (initial request only)

B. CIU: Member’s chart or medical record showing an inadequate treatment response to a second-generation H1 antihistamine (initial request only)

III. CRITERIA FOR INITIAL APPROVAL

A. Asthma

Authorization of 6 months may be granted for treatment of asthma when all of the following criteria are met:

1. Member is 6 years of age or older.
2. Member has a positive skin test or in vitro reactivity to at least one perennial aeroallergen.
3. Member has a pre-treatment IgE level greater than or equal to 30 IU/mL.
4. Member has inadequate asthma control (e.g., hospitalization or emergency medical care visit within the past year) despite current treatment with both of the following medications at optimized doses:
   a. Inhaled corticosteroid
b. Additional controller (long acting beta₂-agonist, leukotriene modifier, or sustained-release theophylline)
5. Member will not use Xolair as monotherapy.
6. Member does not currently smoke.
7. Member will not use Xolair concomitantly with other biologics (e.g., Cinqair, Dupixent, Fasenra, Nucala).

B. Chronic idiopathic urticaria
Authorization of 6 months may be granted for treatment of chronic idiopathic urticaria when all of the following criteria are met:
1. Member is 12 years of age or older.
2. Member remains symptomatic despite treatment with a second-generation H₁ antihistamine (e.g., cetirizine, fexofenadine, levocetirizine, loratadine) for at least 2 weeks.
3. Member has been evaluated for other causes of urticaria, including bradykinin-related angioedema and interleukin-1-associated urticarial syndromes (auto-inflammatory disorders, urticarial vasculitis).
4. Member has experienced a spontaneous onset of wheals, angioedema, or both, for at least 6 weeks.

IV. CONTINUATION OF THERAPY

A. Asthma
Authorization of 12 months may be granted for treatment of asthma when all of the following criteria are met:
1. Member is 6 years of age or older.
2. Asthma control has improved on Xolair treatment as demonstrated by at least one of the following:
   a. A reduction in the frequency and/or severity of symptoms and exacerbations
   b. A reduction in the daily maintenance oral corticosteroid dose
3. Member will not use Xolair as monotherapy.
4. Member does not currently smoke.
5. Member will not use Xolair concomitantly with other biologics (e.g., Cinqair, Dupixent, Fasenra, Nucala).

B. Chronic idiopathic urticaria
Authorization of 12 months may be granted for continuation of treatment of chronic idiopathic urticaria when all of the following criteria are met:
1. Member is 12 years of age or older.
2. Member has experienced a response (e.g., improved symptoms, decrease in weekly urticaria activity score [UAS7]) since initiation of therapy.

V. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT

XOSPATA (gilteritinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Xospata is indicated for the treatment of adult patients who have relapsed or refractory acute myeloid leukemia (AML) with a FLT3 mutation as detected by an FDA-approved test.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Acute Myeloid Leukemia (AML)
Authorization of 12 months may be granted to adult members for the treatment of FLT3 mutation-positive relapsed or refractory AML.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

Specialty Guideline Management

XPOVIO (selinexor)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Xpovio is indicated in combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, at least two immunomodulatory agents, and an anti-CD38 monoclonal antibody.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Multiple Myeloma
Authorization of 12 months may be granted for the treatment of relapsed or refractory multiple myeloma in members who meet all of the following:
A. Xpovio will be used in combination with dexamethasone
B. The member has received at least four prior therapy regimens
C. The member is refractory to at least two proteasome inhibitors
D. The member is refractory to at least two immunomodulatory agents
E. The member is refractory to an anti-CD38 monoclonal antibody

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced an unacceptable toxicity or disease progression.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

XTANDI (enzalutamide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Xtandi is indicated for the treatment of patients with castration-resistant prostate cancer.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 24 months may be granted to members for the treatment of prostate cancer.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

YERVOY (ipilimumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Yervoy is indicated for the treatment of unresectable or metastatic melanoma in adults and pediatric patients (12 years and older).
2. Yervoy is indicated for the adjuvant treatment of patients with cutaneous melanoma with pathologic involvement of regional lymph nodes of more than 1 mm who have undergone complete resection, including total lymphadenectomy.
3. Yervoy is indicated for the treatment of patients with intermediate or poor risk, previously untreated advanced renal cell carcinoma, in combination with nivolumab.
4. Yervoy is indicated for the treatment of adult and pediatric patients (12 years and older) with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan, in combination with nivolumab.

B. Compendial Uses

1. Retreatment of melanoma in patients who experience disease control but who relapse or progress greater than 3 months after treatment discontinuation
2. Treatment of metastatic or unresectable uveal melanoma as single-agent therapy or in combination with nivolumab
3. Treatment of previously untreated, unresectable or metastatic melanoma in combination with dacarbazine
4. Treatment of metastatic or unresectable cutaneous melanoma as a single agent or in combination with nivolumab
5. Treatment of brain metastases with melanoma as a single agent or in combination with nivolumab
6. Small cell lung cancer subsequent systemic therapy in combination with nivolumab
7. Non-small cell lung cancer in combination with nivolumab

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Melanoma

1. Authorization of 12 months may be granted for the treatment of unresectable or metastatic melanoma.
2. Authorization of 12 months may be granted for the adjuvant treatment of melanoma.
3. Authorization of 12 months may be granted for the treatment of brain metastases with a diagnosis of melanoma.

B. Small Cell Lung Cancer
Authorization of 12 months may be granted for the treatment of small cell lung cancer.

C. Renal Cell Carcinoma
Authorization of 12 months may be granted for the treatment of renal cell carcinoma in combination with nivolumab.

D. Colorectal Cancer
Authorization of 12 months may be granted for the treatment of microsatellite instability-high or mismatch repair deficient colorectal cancer in combination with nivolumab.

E. Non-small Cell Lung Cancer
Authorization of 12 months may be granted for the treatment of non-small cell lung cancer.

III. CONTINUATION OF THERAPY

A. Melanoma
1. Authorization of 12 months may be granted for the treatment of unresectable or metastatic melanoma if the member had disease progression or relapse after stable disease of at least three months duration after their first course of Yervoy.
2. Authorization of 12 months may be granted for the adjuvant treatment of melanoma when the member meets all initial authorization criteria.
3. Authorization of 12 months may be granted for the treatment of brain metastases with a diagnosis of melanoma when the member meets all initial authorization criteria.

B. All Other Indications
Authorization of 12 months may be granted when the member meets all initial authorization criteria.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

YESCARTA (axicabtagene ciloleucel)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Yescarta is a CD19-directed genetically modified autologous T-cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (NOS), primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma.

Limitations of use: Yescarta is not indicated for the treatment of patients with primary central nervous system lymphoma.

B. Compendial Uses

1. Acquired immunodeficiency syndrome (AIDS)-related diffuse large B-cell lymphoma
2. Diffuse large B-cell lymphoma
3. Human herpesvirus 8 (HHV8)-positive diffuse large B-cell lymphoma, NOS
4. Monomorphic post-transplant lymphoproliferative disorder (B-cell type)

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Testing or analysis confirming CD19 protein on the surface of the B-cell.

III. CRITERIA FOR INITIAL APPROVAL

Adult B-cell lymphomas

Authorization of 3 months may be granted for treatment of B-cell lymphomas in members 18 years of age or older when all of the following criteria are met:

A. Member has any of the following B-cell lymphoma subtypes:
   1. Diffuse large B-cell lymphoma (DLBCL) arising from follicular lymphoma (also known as follicular lymphoma with histologic transformation to DLBCL)
   2. Diffuse large B-cell lymphoma
   3. Primary mediastinal large B-cell lymphoma
   4. High-grade B-cell lymphoma (high-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 [double/triple hit lymphoma], high-grade B-cell lymphoma, NOS)
   5. Acquired immunodeficiency syndrome (AIDS)-related diffuse large B-cell lymphoma
6. Human herpesvirus 8 (HHV8)-positive diffuse large B-cell lymphoma, NOS
7. Monomorphic post-transplant lymphoproliferative disorder (B-cell type)

B. The member does not have primary central nervous system lymphoma.
C. The member has not received a previous treatment course of Yescarta or another CD19-directed chimeric antigen receptor (CAR) T-cell therapy.
D. The B-cells must be CD19-positive as confirmed by testing or analysis
E. For diffuse large B-cell lymphoma arising from follicular lymphoma: member received prior treatment with two or more chemoimmunotherapy regimens which included at least one anthracycline or anthracenedione-based regimen, unless contraindicated.
F. For all other B-cell lymphoma subtypes: member has partial response following second-line therapy OR the disease is in second relapse or greater.

IV. REFERENCES
POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Yonsa is indicated in combination with methylprednisolone for the treatment of patients with metastatic castration-resistant prostate cancer (CRPC).

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided if the requested medication is used in combination with a second-generation oral anti-androgen (e.g., apalutamide [Erleada]) or an oral androgen metabolism inhibitor (e.g., abiraterone acetate [Zytiga]).

III. CRITERIA FOR INITIAL APPROVAL

Metastatic castration-resistant prostate cancer
Authorization of 12 months may be granted for treatment of metastatic castration-resistant prostate cancer when the member has had a bilateral orchiectomy or will be using the requested medication in combination with a GnRH analog.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

ZALTRAP (ziv-aflibercept)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Zaltrap is indicated for use in combination with 5-fluorouracil, leucovorin, and irinotecan (FOLFIRI) in patients with metastatic colorectal cancer (mCRC) that is resistant to or has progressed following an oxaliplatin-containing regimen.

B. Compendial Uses

1. Colorectal cancer with unresectable metachronous metastases and previous adjuvant FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin) within the past 12 months, as primary treatment in combination with irinotecan

2. Colorectal cancer, unresectable advanced or metastatic disease in combination with irinotecan or with FOLFIRI regimen not previously treated with irinotecan-based therapy, as subsequent therapy for disease progression

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Colorectal cancer (CRC)

Authorization of 12 months may be granted for treatment of metastatic CRC in combination with 5-fluorouracil, leucovorin, and irinotecan (FOLFIRI) or in combination with irinotecan.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

ZEJULA (niraparib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Zejula indicated for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for maintenance treatment of recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer when the member is in a complete or partial response to platinum-based chemotherapy.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

ZELBORAF (vemurafenib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Zelboraf is indicated for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test.
      Limitation of use: Zelboraf is not indicated for treatment of patients with wild-type BRAF melanoma.
   2. Zelboraf is indicated for the treatment of patients with Erdheim-Chester Disease with BRAF V600 mutation.

B. Compendial Uses
   1. Brain metastases with melanoma in combination with cobimetinib
   2. Non-small cell lung cancer, BRAF V600E mutation-positive
   3. Hairy cell leukemia
   4. Thyroid carcinoma – papillary carcinoma, follicular carcinoma, Hurthle cell carcinoma, BRAF mutation-positive
   5. Glioma, BRAF V600 activating mutation-positive
   6. Meningioma, BRAF V600 activating mutation-positive
   7. Astrocytoma, BRAF V600 activating mutation-positive
   8. Rectal cancer, BRAF V600E mutation-positive
   9. Colon cancer, BRAF V600E mutation-positive
   10. Unresectable or metastatic cutaneous melanoma, BRAF V600 activating mutation-positive

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of BRAF mutation documentation is necessary to initiate the prior authorization review for applicable indications as outlined in Section III.

III. CRITERIA FOR INITIAL APPROVAL

A. Melanoma
   1. Authorization of 12 months may be granted for treatment of unresectable or metastatic melanoma with a BRAF V600 activating mutation (e.g., BRAF V600E or V600K mutation).
   2. Authorization of 12 months may be granted for the treatment of brain metastases with melanoma when all of the following criteria are met:
i. Zelboraf is used in combination with cobimetinib
ii. Tumor is positive for BRAF V600 activating mutation (e.g., BRAF V600E or V600K mutation).

B. Erdheim-Chester Disease (ECD)
Authorization of 12 months may be granted for treatment of ECD with BRAF V600 mutation.

C. Non-small Cell Lung Cancer (NSCLC)
Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive NSCLC.

D. Hairy Cell Leukemia
Authorization of 12 months may be granted for treatment of hairy cell leukemia.

E. Thyroid Carcinoma (follicular, Hürthle cell, papillary)
Authorization of 12 months may be granted for treatment of BRAF mutation-positive radioiodine refractory papillary carcinoma, follicular carcinoma, or Hürthle cell carcinoma.

F. Central Nervous System Cancer
Authorization of 12 months may be granted for treatment of BRAF V600 mutation-positive gliomas, menigiomas, or astrocytomas.

G. Rectal Cancer
Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive rectal cancer.

H. Colon Cancer
Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive colon cancer.

IV. CONTINUATION OF THERAPY
Authorization of 12 months may be granted for continuation of therapy for an indication outlined in Section III when there is no evidence of unacceptable toxicity or disease progression on the current regimen.

V. REFERENCES


SPECIALTY GUIDELINE MANAGEMENT
ZEPATIER (elbasvir and grazoprevir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   Zepatier is indicated for the treatment of chronic hepatitis C virus genotype 1 or 4 infection in adults. Zepatier is indicated for use with ribavirin in certain patient populations.

B. Compendial Uses
   Chronic hepatitis C genotype 3 infection

All other indications are considered experimental/investigational and are not a covered benefit.

II. EXCLUSIONS

Coverage will not be provided for members with decompensated cirrhosis/moderate or severe hepatic impairment (Child Turcotte Pugh Class B or C)

Note: When the requested drug is being used in a combination therapy regimen, exclusions to the other antiviral drugs also apply.

III. CRITERIA FOR APPROVAL

A. Chronic hepatitis C virus infection, in combination with ribavirin (RBV)
   1. Genotype 1a infection
      a. Authorization of up to 16 weeks total may be granted for members with baseline NS5A resistance-associated substitutions (RASs)/polymorphisms (see Section V) who are either of the following:
         i. Treatment-naïve
         ii. Failed prior treatment with peginterferon alfa (PEG-IFN) and RBV with or without an HCV protease inhibitor (boceprevir, simeprevir or telaprevir)
      b. Authorization of up to 12 weeks total may be granted for members without baseline NS5A resistance-associated substitutions (RASs)/polymorphisms (see Section V) who have failed prior treatment with PEG-IFN and RBV with an HCV protease inhibitor (boceprevir, simeprevir or telaprevir).
   2. Genotype 1b infection
      Authorization of up to 12 weeks total may be granted for members who failed prior treatment with PEG-IFN and RBV with an HCV protease inhibitor (boceprevir, simeprevir or telaprevir).
   3. Genotype 4 infection
Authorization of up to 16 weeks total may be granted for members who failed prior treatment with PEG-IFN and RBV.

**B. Chronic hepatitis C virus infection, without RBV**

1. **Genotype 1a infection**
   a. Authorization of up to 12 weeks total may be granted for members with end-stage renal disease (ESRD) or severe renal impairment (estimated glomerular filtration rate [eGFR] of less than 30 ml/min/1.73m²).
   b. Authorization of up to 12 weeks total may be granted for members without baseline NS5A resistance-associated substitutions (RASs)/polymorphisms who are either of the following:
      i. Treatment-naïve
      ii. Failed prior treatment with PEG-IFN and RBV without an HCV protease inhibitor (boceprevir, simeprevir or telaprevir)

2. **Genotype 1b infection**
   Authorization of up to 12 weeks total may be granted for members who are either of the following:
   a. Treatment-naïve
   b. Failed prior treatment with PEG-IFN and RBV without an HCV protease inhibitor (boceprevir, simeprevir or telaprevir)

3. **Genotype 4 infection**
   Authorization of up to 12 weeks total may be granted for members who are either of the following:
   a. Treatment-naïve
   b. Failed prior treatment with PEG-IFN and RBV

**C. Chronic hepatitis C virus infection, in combination with Sovaldi**

**Genotype 3 infection**

Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV.

**D. HCV and HIV coinfection**

Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A, B or C above are met.

**IV. CONTINUATION OF THERAPY**

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

**V. APPENDIX: NS5A RESISTANCE-ASSOCIATED SUBSTITUTIONS (POLYMORPHISMS)**

NS5A resistance-associated substitutions (polymorphisms) at amino acid positions M28, Q30, L31 or Y93. Examples include M28A/T, Q30H/R, L31M/V, and Y93C/H/N.

**VI. REFERENCES**

SPECIALTY GUIDELINE MANAGEMENT

ZINBRYTA (daclizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication: Zinbryta is indicated for the treatment of adult patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of Zinbryta should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Multiple Sclerosis
Authorization of 24 months may be granted to members with a diagnosis of a relapsing form of multiple sclerosis who have had an inadequate response to two or more drugs indicated for multiple sclerosis.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

ZOLADEX (goserelin acetate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Prostate cancer
      a. For use in combination with flutamide for the management of locally confined stage T2b-T4 (Stage B2-C) carcinoma of the prostate. Treatment with Zoladex and flutamide should start 8 weeks prior to initiating radiation therapy and continue during radiation therapy.
      b. In the palliative treatment of advanced carcinoma of the prostate
   2. Endometriosis
      For the management of endometriosis, including pain relief and reduction of endometriotic lesions for the duration of therapy. Experience with Zoladex for the management of endometriosis has been limited to women 18 years of age and older treated for 6 months (Zoladex 3.6 mg strength only)
   3. Endometrial thinning
      For use as an endometrial-thinning agent prior to endometrial ablation for dysfunctional uterine bleeding (Zoladex 3.6 mg strength only)
   4. Advanced breast cancer
      For use in the palliative treatment of advanced breast cancer in pre-and perimenopausal women

B. Compendial Uses
   1. Breast cancer
   2. Prostate cancer
   3. Gender dysphoria (also known as gender non-conforming or transgender persons)

   NOTE: Some plans may opt-out of coverage for gender dysphoria.

All other indications are considered experimental/investigational and are not a covered benefit.

II. EXCLUSIONS

Coverage will not be provided for members with any of the following exclusions: Use of the 10.8 mg strength for diagnoses other than prostate cancer, breast cancer, and gender dysphoria (if applicable).

III. CRITERIA FOR INITIAL APPROVAL

A. Breast Cancer
   Authorization of 12 months may be granted for the treatment of HR-positive breast cancer.

B. Prostate Cancer
Authorization of 12 months may be granted for treatment of prostate cancer.

C. Endometriosis
Authorization of 6 months may be granted for treatment of endometriosis.

D. Endometrial-thinning agent
Authorization of 2 doses may be granted for endometrial thinning prior to endometrial ablation for dysfunctional uterine bleeding.

E. Gender Dysphoria
1. Authorization of 12 months may be granted for pubertal suppression in preparation for gender reassignment in an adolescent member when all of the following criteria are met:
   a. The member has a diagnosis of gender dysphoria.
   b. The member has reached Tanner stage 2 of puberty.
2. Authorization of 12 months may be granted for gender reassignment in an adult member when all of the following criteria are met:
   a. The member has a diagnosis of gender dysphoria.
   b. The member will receive Zoladex concomitantly with cross sex hormones.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

RECLAST (zoledronic acid)

zoledronic acid

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Treatment and prevention of osteoporosis in postmenopausal women
   2. Treatment to increase bone mass in men with osteoporosis
   3. Treatment and prevention of glucocorticoid-induced osteoporosis
   4. Treatment of Paget’s disease of bone in men and women

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Supporting chart notes or medical record indicating a history of fractures, T-score, and FRAX fracture probability as applicable to Sections III.A, III.B, and III.C.

III. CRITERIA FOR INITIAL APPROVAL

A. Postmenopausal osteoporosis
   Authorization of 12 months may be granted to postmenopausal members with osteoporosis when ANY of the following criteria are met:
   1. Member has a history of fragility fractures
   2. Member has a pre-treatment T-score less than or equal to -2.5 OR member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B) and meets ANY of the following criteria:
      a. Member has indicators of higher fracture risk (e.g., advanced age, frailty, glucocorticoid use, very low T-scores [less than or equal to -3.5], or increased fall risk)
      b. Member has failed prior treatment with or is intolerant to previous injectable osteoporosis therapy (e.g., denosumab [Prolia], teriparatide [Forteo])
      c. Member has had an oral bisphosphonate trial of at least 1-year duration or there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)

B. Osteoporosis in men
   Authorization of 12 months may be granted to male members with osteoporosis when ANY of the following criteria are met:
1. Member has a history of an osteoporotic vertebral or hip fracture
2. Member meets criteria BOTH of the following criteria:
   a. Member has a pre-treatment T-score less than or equal to -2.5 OR member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B)
   b. Member has had an oral bisphosphonate trial of at least 1-year duration OR there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)

C. Glucocorticoid-induced osteoporosis
Authorization of 12 months may be granted for members with glucocorticoid-induced osteoporosis when ALL of the following criteria are met:
1. Member has had an oral bisphosphonate trial of at least 1-year duration OR there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)
2. Member is currently receiving or will be initiating glucocorticoid therapy
3. Member meets ANY of the following criteria:
   a. Member has a history of a fragility fracture
   b. Member has a pre-treatment T-score of less than or equal to -2.5
   c. Member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B)

D. Paget’s disease of bone
Authorization of one dose (5 mg) may be granted for the treatment of Paget’s disease of bone.

IV. CONTINUATION OF THERAPY
A. Paget’s disease of bone
   All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

B. All other indications
   Authorization of 12 months may be granted for all members (including new members) who meet all initial authorization criteria and experiences clinical benefit after at least 24 months of therapy with zoledronic acid or Reclast as evidenced by improvement or stabilization in T-score.

V. APPENDIX
   Appendix A. Clinical reasons to avoid oral bisphosphonate therapy
   • Esophageal abnormality that delays emptying such as stricture of achalasia
   • Active upper gastrointestinal problem (e.g., dysphagia, gastritis, duodenitis, erosive esophagitis, ulcers)
   • Inability to stand or sit upright for at least 30 to 60 minutes
   • Inability to take at least 30 to 60 minutes before first food, drink, or medication of the day
   • Renal insufficiency (creatinine clearance <35 mL/min)
   • History of intolerance to an oral bisphosphonate

   Appendix B. WHO Fracture Risk Assessment Tool
   • High FRAX fracture probability: 10 year major osteoporotic fracture risk ≥ 20% or hip fracture risk ≥ 3%
   • 10-year probability; calculation tool available at: https://www.sheffield.ac.uk/FRAX/
   • The estimated risk score generated with FRAX should be multiplied by 1.15 for major osteoporotic fracture and 1.2 for hip fracture if glucocorticoid treatment is greater than 7.5 mg per day.
VI. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

ZOMETA (zoledronic acid)
zoledronic acid

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Zometa/zoledronic acid is indicated for the treatment of hypercalcemia of malignancy defined as an albumin-corrected calcium (cCa) of greater than or equal to 12mg/dL [3.0 mmol/L] using the formula: cCa in mg/dL=Ca in mg/dL + 0.8 (4.0 g/dL – patient albumin [g/dL]).

2. Zometa/zoledronic acid is indicated for the treatment of patients with multiple myeloma and patients with documented bone metastases from solid tumors, in conjunction with standard antineoplastic therapy. Prostate cancer should have progressed after treatment with at least one hormonal therapy.

Limitation of Use: The safety and efficacy of Zometa/zoledronic acid in the treatment of hypercalcemia associated with hyperparathyroidism or with other non-tumor-related conditions have not been established.

B. Compendial Uses

1. Treatment or prevention of osteoporosis during androgen-deprivation therapy (ADT) in prostate cancer patients with high fracture risk

2. Treatment in postmenopausal patients with breast cancer who are receiving adjuvant therapy to maintain or improve bone mineral density and reduce risk of fractures

3. Treatment for osteopenia or osteoporosis in patients with systemic mastocytosis

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Hypercalcemia of Malignancy

Authorization of 2 months may be granted for members who are prescribed zoledronic acid or Zometa for hypercalcemia of malignancy.

B. Multiple Myeloma

Authorization of 12 months may be granted for members who are prescribed zoledronic acid or Zometa for multiple myeloma.

C. Bone Metastases from a Solid Tumor

Authorization of 12 months may be granted for members who are prescribed zoledronic acid or Zometa for bone metastases from a solid tumor.
D. Prostate Cancer
Authorization of 12 months may be granted for members with prostate cancer who are prescribed zoledronic acid or Zometa for the treatment or prevention of osteoporosis during androgen deprivation therapy (ADT)

E. Breast Cancer
Authorization of 12 months may be granted for postmenopausal (natural or induced) members who are receiving adjuvant therapy for the treatment of breast cancer and are prescribed zoledronic acid or Zometa to maintain or improve bone mineral density and reduce the risk of fractures.

F. Systemic Mastocytosis
Authorization of 12 months may be granted for members who are prescribed zoledronic acid or Zometa for the treatment of osteopenia or osteoporosis in members with systemic mastocytosis.

III. CONTINUATION OF THERAPY

A. Hypercalcemia of malignancy
Authorization of 2 months will be granted for continued treatment in members requesting reauthorization for hypercalcemia of malignancy who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

B. All Diagnosis (excluding hypercalcemia of malignancy)
Authorization of 12 months will be granted for continued treatment in members requesting reauthorization for an indication listed in Section II (excluding hypercalcemia of malignancy) who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

ZOLGENSMA (abeparvovec-xioi)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Zolgensma is indicated for the treatment of pediatric patients less than 2 years of age with spinal muscular atrophy (SMA) with bi-allelic mutations in the survival motor neuron (SMN1) gene.

Limitations of use:
- The safety and effectiveness of repeat administrations of Zolgensma have not been evaluated.
- The use of Zolgensma in patients with advanced SMA (e.g., complete paralysis of limbs, permanent ventilator dependence) has not been evaluated.

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
Genetic testing results demonstrating bi-allelic mutations in the survival motor neuron 1 (SMN1) gene

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a physician who specializes in treatment of spinal muscular atrophy.

IV. CRITERIA FOR INITIAL APPROVAL

Spinal muscular atrophy
Authorization of one dose total may be granted for treatment of spinal muscular atrophy when all of the following criteria are met:
1. Member has a genetically confirmed diagnosis of SMA, with documentation of bi-allelic mutations in the survival motor neuron 1 (SMN1) gene (deletions or point mutations).
2. Member is less than 2 years of age.
3. Member does not have advanced SMA, including but not limited to any of the following:
   a. Complete paralysis of limbs
   b. Invasive ventilatory support (tracheostomy)
c. Respiratory assistance for 16 or more hours per day (including non-invasive respiratory support) continuously for 14 or more days in the absence of acute reversible illness (excluding perioperative ventilation)

4. The member has an anti-adenovirus-associated virus 9 (AAV9) antibody titer less than or equal to 1:50 as determined by Enzyme-linked Immunosorbent Assay (ELISA) binding immunoassay.

5. If the member is on nusinersen (Spinraza), it will be discontinued prior to administration of the requested drug.

6. The member has not received Zolgensma previously.

V. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

ZOLINZA (vorinostat)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
   Treatment of cutaneous manifestations in patients with cutaneous T-cell lymphoma who have progressive, persistent, or recurrent disease on or following two systemic therapies

B. Compendial Uses
   1. Mycosis fungoides (MF)
   2. Sézary syndrome (SS)

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR APPROVAL

Cutaneous T-cell Lymphoma (CTCL)
Authorization of 12 months may be granted for the treatment of CTCL (e.g., MF, SS).

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

ZORBTIVE (somatropin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Zorbtive is indicated for the treatment of short bowel syndrome in adult patients receiving specialized nutritional support. Zorbtive should be used in conjunction with optimal management of short bowel syndrome.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Short bowel syndrome (SBS)
Authorization of a total of 8 weeks may be granted to members who are prescribed Zorbtive for the treatment of SBS.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

ZULRESSO (brexanolone)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Treatment of postpartum depression (PPD) in adults

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 1 infusion may be granted for treatment of moderate to severe postpartum depression in members 18 years of age or older when all of the following criteria are met:
A. Member has had a major depressive episode that began no earlier than the third trimester of pregnancy and no later than the first 4 weeks following delivery, documented by standardized rating scales that reliably measure depressive symptoms (e.g., Beck Depression Scale [BDI], Hamilton Depression Rating Scale [HDRS], Montgomery-Asberg Depression Rating Scale [MADRS], etc.)
B. Diagnosis is verified by a psychiatrist
C. Member is 6 months postpartum or less
D. Lactation has ceased or breastmilk produced will not be used for feedings during the infusion and up to 4 days following infusion completion
E. Member does not have current substance or alcohol use disorder
F. Member will not receive more than one infusion per pregnancy/childbirth

III. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

ZYDELG (idelalisib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Relapsed chronic lymphocytic leukemia (CLL), in combination with rituximab, in patients for whom rituximab alone would be considered appropriate therapy due to other co-morbidities
2. Relapsed follicular B-cell non-Hodgkin lymphoma (FL) in patients who have received at least two prior systemic therapies
3. Relapsed small lymphocytic lymphoma (SLL) in patients who have received at least two prior systemic therapies

Limitations of use:
Zydelig is not indicated and is not recommended for first-line treatment of any patient.
Zydelig is not indicated and is not recommended in combination with bendamustine and/or rituximab for the treatment of FL.

Accelerated approval for FL and SLL was granted based on overall response rate. Improvement in patient survival or disease related symptoms has not been established. Continued approval for these indications may be contingent upon verification of clinical benefit in confirmatory trials.

B. Compendial Uses

1. Relapsed or refractory CLL/SLL
2. Refractory or relapsed follicular lymphoma
3. Marginal zone lymphomas (nodal, splenic, gastric MALT and non-gastric MALT)

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)

Authorization of 12 months may be granted for treatment CLL/SLL when either of the following criteria are met:
   a. Zydelig will be used as a single agent, or
   b. Zydelig will be used in combination with rituximab.

B. Follicular B-cell non-Hodgkin lymphoma (FL)

Authorization of 12 months may be granted for treatment of FL in patients who have received at least two prior systemic therapies for their disease.
C. Marginal zone lymphomas
Authorization of 12 months may be granted for treatment of marginal zone lymphoma (nodal, splenic, gastric MALT, and non-gastric MALT) in patients who have received at least two prior systemic therapies for their disease.

III. CONTINUATION OF THERAPY
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

ZYKADIA (ceritinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

ZYkadia is indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test.

B. Compendial Uses

1. NSCLC, recurrent, advanced or metastatic ALK rearrangement-positive or ROS1 rearrangement-positive tumors
2. Inflammatory myofibroblastic tumor (IMT) with ALK translocation
3. Recurrent brain metastases from ALK-positive NSCLC

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: ALK mutation or translocation status or ROS-1 mutation status (where applicable).

III. CRITERIA FOR INITIAL APPROVAL

A. Non-small cell lung cancer (NSCLC)

Authorization of 12 months may be granted for treatment of NSCLC when the member meets either of the following criteria:

1. Member has recurrent, advanced or metastatic ALK-positive NSCLC (including brain metastases from NSCLC).
2. Member has recurrent, advanced or metastatic ROS1-positive NSCLC.

B. Inflammatory myofibroblastic tumor (IMT)

Authorization of 12 months may be granted for treatment of ALK-positive IMT.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication in Section III who have not experienced disease progression or an unacceptable toxicity.
V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

ZYTIGA (abiraterone)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

1. Zytiga is indicated in combination with prednisone for the treatment of patients with metastatic castration-resistant prostate cancer.
2. Zytiga is indicated in combination with prednisone for the treatment of patients with metastatic high-risk castration-sensitive prostate cancer.

B. Compendial Uses

Node-positive (N1), non-metastatic (M0) prostate cancer

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 24 months may be granted for the treatment of prostate cancer.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES