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
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), (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

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

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 (a) or criterion (b) below:
   i. Recurrent or persistent CTEPH after pulmonary endarterectomy (PEA)
   ii. Inoperable CTEPH with diagnosis confirmed by BOTH of the following (i. and ii.):
      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 PAH or CTEPH who are currently receiving Adempas therapy through a paid pharmacy or medical benefit.

IV. APPENDIX

WHO Classification of Pulmonary Hypertension

WHO Group 1. Pulmonary Arterial Hypertension (PAH)

1.1 Idiopathic (IPAH)

1.2 Heritable PAH
   1.2.1 Germline mutations in the bone morphogenetic protein receptor type 2 (BMPR2)
   1.2.2 Activin receptor-like kinase type 1 (ALK1), endoglin (with or without hereditary hemorrhagic telangiectasia), Smad 9, caveolin-1 (CAV1), potassium channel super family K member-3 (KCNK3)
   1.2.3 Unknown

1.3 Drug- and toxin-induced

1.4. 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. Pulmonary veno-occlusive disease (PVOD) and/or pulmonary capillary hemangiomatosis (PCH)

1. Persistent pulmonary hypertension of the newborn (PPHN)

WHO Group 2. Pulmonary Hypertension Owing to Left Heart Disease

2.1 Systolic dysfunction

2.2 Diastolic dysfunction

2.3 Valvular disease

2.4 Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies

WHO Group 3. Pulmonary Hypertension Owing to Lung Disease and/or Hypoxia

3.1 Chronic obstructive pulmonary disease

3.2 Interstitial lung disease

3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern

3.4 Sleep-disordered breathing

3.5 Alveolar hypoventilation disorders

3.6 Chronic exposure to high altitude

3.7 Developmental abnormalities

WHO Group 4. Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

WHO Group 5. Pulmonary Hypertension with Unclear Multifactorial Mechanisms

5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders, splenectomy

5.2 Systemic disorders: sarcoidosis, pulmonary Langerhans cell histiocytosis: lymphangioleiomyomatosis, neurofibromatosis, vasculitis

5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders

5.4 Others: tumoral obstruction, fibrosing mediastinitis, chronic renal failure on dialysis, segmental PH
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. 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. Adults with progressive neuroendocrine tumors of pancreatic origin (pNETs) that are unresectable, locally advanced or metastatic
   3. Adults with advanced renal cell carcinoma (RCC) after failure of treatment with sunitinib or sorafenib
   4. Adults with renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery
   5. Adults with progressive, well-differentiated, non-functional neuroendocrine tumors of gastrointestinal or lung origin that are unresectable, locally advanced or metastatic
   6. Adults and pediatric patients with tuberous sclerosis complex (TSC) who have subependymal giant cell astrocytoma (SEGA) that requires therapeutic intervention but cannot be curatively resected.

B. Compendial Uses
   1. Relapse or stage IV RCC:
      a. Systemic therapy for non-clear cell histology
      b. Subsequent therapy for predominant clear cell histology
   2. Soft tissue sarcoma subtypes:
      a. Perivascular epithelioid cell tumors (PEComa)
      b. Recurrent angiomyolipoma
      c. Lymphangioleiomyomatosis
   3. Neuroendocrine tumor of the thymus
   4. Thymomas and thymic carcinomas
   5. Osteosarcoma
   6. Classical Hodgkin lymphoma
   7. Papillary, Hürthle cell, and follicular thyroid carcinoma
   8. Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma

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 HR-positive, HER2-negative recurrent or metastatic breast cancer when prescribed in combination with exemestane and any of the following criteria are met:
1. Member has been previously treated with tamoxifen
2. Disease has progressed while on or within 12 months of therapy with a nonsteroidal aromatase inhibitor

B. Renal Cell Carcinoma
Authorization of 12 months may be granted for treatment of relapsed, metastatic, or unresectable RCC when either of the following criteria are met:
1. Disease is of non-clear cell histology
2. Disease is of predominantly clear cell histology and has progressed on prior antiangiogenic therapy (e.g., Avastin, Sutent, Votrient).

C. Neuroendocrine Tumors
Authorization of 12 months may be granted for treatment of neuroendocrine tumors of pancreatic gastrointestinal, lung, or thymic origin.

D. Renal Angiomyolipoma Associated With Tuberous Sclerosis Complex (TSC)
Authorization of 12 months may be granted for treatment of renal angiomyolipoma associated with TSC.

E. Subependymal Giant Cell Astrocytoma (SEGA) Associated With Tuberous Sclerosis Complex (TSC)
Authorization of 12 months may be granted for treatment of SEGA associated with TSC.

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

G. Thymomas and Thymic Carcinomas
Authorization of 12 months may be granted for treatment of thymomas and thymic carcinomas.

H. Osteosarcoma
Authorization of 12 months may be granted for treatment of osteosarcoma.

I. Classical Hodgkin Lymphoma
Authorization of 12 months may be granted for treatment of classical Hodgkin lymphoma.

J. Waldenström’s Macroglobulinemia/Lymphoplasmacytic Lymphoma
Authorization of 12 months may be granted for treatment of Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma.

K. Thyroid Carcinoma
Authorization of 12 months may be granted for treatment of thyroid carcinoma with any of the following histologies: papillary, Hurthle cell, follicular.
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

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

1. What is the patient’s diagnosis?
   a. Alpha-antitrypsin (AAT) deficiency → Go to #2
   b. Other → Deny – Coverage for alpha1-proteinase inhibitors is provided when the patient has alpha1-antitrypsin (AAT) deficiency. The information provided by the prescriber does not indicate that this condition is met. Based on the information provided by the prescriber, use of alpha1-proteinase inhibitors is not covered by the plan.
      [Short description: Not an approvable diagnosis]

2. Does the patient have clinically evident emphysema?
   a. Yes → Go to #3
   b. No → Deny - Coverage for alpha1-proteinase inhibitors for alpha1-antitrypsin (AAT) deficiency is provided when the patient has clinically evident emphysema. The information provided by the prescriber does not indicate that this condition is met. Based on the information provided by the prescriber, use of alpha1-proteinase inhibitors is not covered by the plan.
      [Short description: No emphysema]

3. Is the patient’s pretreatment post-bronchodilation FEV1 (forced expiratory volume in 1 second) between 25% and 80% of the predicted value?
   a. Yes → Go to #4
   b. No → Deny - Coverage for alpha1-proteinase inhibitors for alpha1-antitrypsin (AAT) deficiency is provided when the patient’s pretreatment post-bronchodilation FEV1 (forced expiratory volume in 1 second) is between 25% and 80% of the predicted value. The information provided by the prescriber does not indicate that this condition is met. Based on the information provided by the prescriber, use of alpha1-proteinase inhibitors is not covered by the plan.
      [Short description: Pretreatment FEV1]

4. What is the patient’s pretreatment serum AAT level?
   a. Less than 11 micromol/L (80 mg/dL by radial immunodiffusion or 50 mg/dl by nephelometry) → Approve indefinitely
   b. Greater than or equal to 11 micromol/L (80 mg/dL by radial immunodiffusion or 50 mg/dl by nephelometry) → Deny - Coverage for alpha1-proteinase inhibitors for alpha1-antitrypsin (AAT) deficiency is provided when the patient’s pretreatment serum AAT (alpha1-antitrypsin) level is less than 11 micromoles per liter. The information provided by the prescriber does not indicate that this condition is met. Based on the information provided by the prescriber, use of alpha1-proteinase inhibitors is not covered by the plan.
      [Short description: Pretreatment AAT level]
   c. No serum AAT level → Deny - Coverage for alpha1-proteinase inhibitors for alpha1-antitrypsin (AAT) deficiency is provided when the patient’s pretreatment serum AAT (alpha1-antitrypsin) level is less than 11 micromoles per liter. The information provided by the prescriber does not indicate that this condition is met. Based on the information provided by the prescriber, use of alpha1-proteinase inhibitors is not covered by the plan.
      [Short description: No serum AAT level]
level is less than 11 micromoles per liter. The information provided by the prescriber does not indicate that this condition is met. Based on the information provided by the prescriber, use of alpha1-proteinase inhibitors is not covered by the plan.

Document History
Written: Specialty Clinical Development (LH) 10/2006
PRIOR AUTHORIZATION CRITERIA

DRUG CLASS
ANABOLIC STEROIDS

BRAND NAME
(generic)

ANADROL-50
(oxymetholone)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization
Ref # 1087-A

FDA-APPROVED INDICATIONS

Anadrol-50
Anadrol-50 is indicated in the treatment of anemias caused by deficient red cell production. Acquired aplastic anemia, congenital aplastic anemia, myelofibrosis and the hypoplastic anemias due to the administration of myelotoxic drugs often respond. Anadrol tablets should not replace other supportive measures such as transfusion, correction of iron, folic acid, vitamin B₁₂ or pyridoxine deficiency, antibacterial therapy and the appropriate use of corticosteroids.

Compendial Uses
• Cachexia associated with AIDS
• Fanconi’s Anemia

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:
• The requested drug is being prescribed for any of the following: A) Fanconi’s anemia, B) Cachexia associated with AIDS (HIV wasting) or due to chronic disease, C) Anemia due to deficient red-cell production, (e.g. acquired aplastic anemia, congenital aplastic anemia, myelofibrosis, or the hypoplastic anemias due to the administration of myelotoxic drugs)

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. Anadrol-50 (oxymetholone) is indicated in the treatment of anemias caused by deficient red cell production, which include acquired aplastic anemia, congenital aplastic anemia, myelofibrosis and the hypoplastic anemias due to the administration of myelotoxic drugs.

Additionally, oxymetholone produced significant gains in lean body mass and body cell mass in HIV patients with wasting and has also been successful in treating Fanconi’s anemia.³⁶

REFERENCES

Written by: UM Development (GP)
Date Written: 8/1997
Revised: (LS) 12/1998; (MG) 12/2002, 12/2003; (TM) 09/2004; (MC) 10/2005; (MG) 10/2006(2); (NB) 07/2007; (CT) 09/2007; (AM) 09/2008; (CT) 09/2009; (MS) 09/2010, 06/2011, 11/2011, 03/2012; (PL) 06/2012; (CT) 06/2013, 12/2013 (split Anadrol-50 and Oxandrin into separate criteria), 02/2014; (RP) 02/2015; (MS) 02/2016, 02/2017

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**CRITERIA FOR APPROVAL**

1. Is the requested drug being prescribed for any of the following: A) Fanconi’s anemia, B) Cachexia associated with AIDS (HIV wasting) or due to chronic disease, C) Anemia due to deficient red-cell production, (e.g. acquired aplastic anemia, congenital aplastic anemia, myelofibrosis, or the hypoplastic anemias due to the administration of myelotoxic drugs)?

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<th>Yes to question(s)</th>
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<td>Your plan covers this drug when you meet one of these conditions:</td>
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<tr>
<td>- You have anemia due to deficient red-cell production, (e.g. acquired aplastic anemia, congenital aplastic anemia, myelofibrosis, or the hypoplastic anemias due to the administration of myelotoxic drugs)</td>
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<tr>
<td>- You have Fanconi's anemia</td>
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<tr>
<td>- You have AIDS-wasting or cachexia due to chronic disease</td>
<td></td>
</tr>
<tr>
<td>Your use of this drug does not meet these requirements. This is based on the information we have.</td>
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PRIOR AUTHORIZATION CRITERIA

<table>
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<th>DRUG CLASS</th>
<th>ANABOLIC STEROIDS</th>
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<td>BRAND NAME</td>
<td>(generic)</td>
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<tr>
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<td>OXANDRIN</td>
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<td>(oxandrolone)</td>
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Status: CVS Caremark Criteria  
Type: Initial Prior Authorization  
Ref # 15-A

FDA-APPROVED INDICATIONS
Oxandrin
Oxandrolone is indicated as adjunctive therapy to promote weight gain after weight loss following extensive surgery, chronic infections, or severe trauma, and in some patients who without definite pathophysiologic reasons fail to gain or maintain normal weight, to offset the protein catabolism associated with prolonged administration of corticosteroids, and for the relief of bone pain frequently accompanying osteoporosis.

Compendia Uses
- Cachexia associated with AIDS
- To enhance growth in patients with Turner’s Syndrome

COVERAGE CRITERIA
Oxandrin will be covered with prior authorization when the following criteria are met:
- The requested drug is being prescribed for any of the following: A) As adjunctive therapy to promote weight gain after weight loss following extensive surgery, chronic infections or severe trauma, B) To offset the protein catabolism associated with prolonged administration of corticosteroids, C) For the relief of bone pain accompanying osteoporosis, D) To enhance growth in patients with Turner's Syndrome, E) Cachexia associated with AIDS (HIV wasting) or due to chronic 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. Oxandrin is indicated as adjunctive therapy to promote weight gain after weight loss following extensive surgery, chronic infections, or severe trauma, and in some patients who without definite pathophysiologic reasons fail to gain or maintain normal weight, to offset the protein catabolism associated with prolonged administration of corticosteroids, and for the relief of bone pain frequently accompanying osteoporosis.

Some studies have shown that Oxandrin (oxandrolone) may have some beneficial effect as adjunctive therapy for AIDS patients suffering from HIV-wasting syndrome. Use of Oxandrin (oxandrolone) as adjunctive therapy in the treatment of short stature associated with Turner Syndrome is part of the recommendations of the Fifth International Symposium on Turner Syndrome.

REFERENCES


CRITERIA FOR APPROVAL

1. Is the requested drug being prescribed for any of the following: A) As adjunctive therapy to promote weight gain after weight loss following extensive surgery, chronic infections or severe trauma, B) To offset the protein catabolism associated with prolonged administration of corticosteroids, C) For the relief of bone pain accompanying osteoporosis, D) To enhance growth in patients with Turner’s Syndrome, E) Cachexia associated with AIDS (HIV wasting) or due to chronic disease?

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<td><strong>DENIAL REASONS – DO NOT USE FOR MEDICARE PART D</strong></td>
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<tr>
<td>1. Approve, 6 Months</td>
<td>Deny</td>
</tr>
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<td>- Your plan covers this drug when you are using it for one of the following: - As adjunctive therapy to promote weight gain after weight loss following extensive surgery, chronic infections or severe trauma - To offset the protein catabolism associated with prolonged administration of corticosteroids - For the relief of bone pain accompanying osteoporosis - You have Turner’s syndrome - You have AIDS-wasting or cachexia due to chronic disease</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>
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## PRIOR AUTHORIZATION CRITERIA

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<td>BRAND NAME</td>
<td>(generic) benzphetamine products</td>
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<td>diethylpropion products</td>
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<td>phendimetrazine products</td>
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<td>phentermine products (including SUPRENZA)</td>
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</table>

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

### 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.

Phendimetrazine tartrate (PDM) 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. 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 ≥ 30 kg/m², or ≥ 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
Antiobesity agents will be covered with prior authorization when the following criteria are met:
• The patient has not received approval for 3 months of therapy within the past 365 days AND
• The requested medication will be used with a reduced calorie diet and increased physical activity AND
  o The patient has a body mass index (BMI) greater than or equal to 30 kg per square meter OR
  o 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 ≥ 30 kg/m², or ≥ 27 kg/m² in the presence of other risk factors (e.g., hypertension, diabetes, hyperlipidemia). 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. 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 ≥ 30 kg/m² or ≥ 27 kg/m² if other risk factors are present (e.g., hypertension, diabetes, dyslipidemia, sleep apnea, cardiovascular disease).9,10

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. Coverage will be approved for only 3 months per year.

REFERENCES
CRITERIA FOR APPROVAL

1 Has the patient received 3 months of therapy within the past 365 days?  
   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

<table>
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<tr>
<th>Set 1</th>
<th>Duration of Approval</th>
<th>3 Months (90 days of therapy) per year.</th>
<th>Set 2</th>
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Mapping Instructions

<table>
<thead>
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<th>Yes</th>
<th>No</th>
<th>DENIAL REASONS – DO NOT USE FOR MEDICARE PART D</th>
</tr>
</thead>
</table>
| 1   |    | Deny  Go to 2  
Your plan covers this drug when you have not received 3 months of therapy within the past year.  
Your use of this drug does not meet the requirement. This is based on the information we have. |
| 2   |    | Go to 4  Go to 3  
Your plan covers this drug when you have not received 3 months of therapy within the past year.  
Your use of this drug does not meet the requirement. This is based on the information we have. |

Written by: UM Development (LS)
Date Written: 07/1997
Revised: (GP) 6/1998, 06/2000; (JG) 07/2002; (MG) 10/2003; (NB) 11/2004, 07/2005, 06/2006; (CT) 08/2007; (MS) 07/2008; (CT) 08/2010; (KM) 07/2011; (CY) 06/2012; (PL/TM) 06/2013, (PL) 06/2014, 12/2014 (removed “approval of” from question #1); (MG) 07/2015, 12/2015 (updated Q5 to make trade compatible); (SE) 01/2016 (Added guidelines for approval grid); (MS) 07/2016 (removed safety question)
| 3 | Go to 4 | Deny | 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 use of this drug does not meet the requirements. This is based on the information we have. |
|---|---|---|---|
| 4 | Approve for 3 months (90 days of therapy) per year. | Deny | Your plan covers this drug when you will diet and exercise.  
Your use of this drug does not meet the requirement. This is based on the information we have. |
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.

Limitations of Use:
1. Aranesp has not been shown to improve quality of life, fatigue, or patient well-being.
2. Aranesp is not indicated for use:
   • In patients with cancer receiving hormonal agents, biologic products, or radiotherapy, unless also receiving concomitant myelosuppressive chemotherapy.
   • In patients with cancer receiving myelosuppressive chemotherapy when the anticipated outcome is cure.
   • As a substitute for RBC transfusions in patients who require immediate correction of anemia

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 thrombocytemia myelofibrosis

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.

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 non-myeloid malignancy who meet ALL of the following criteria:
1. The intent of chemotherapy is non-curative
2. Pretreatment hemoglobin < 10 g/dL

C. Anemia in MDS
Authorization of 12 weeks may be granted for members with pretreatment hemoglobin < 10 g/dL.
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. Member has symptomatic anemia
2. Pretreatment hemoglobin < 10 g/dL
3. Pretreatment serum erythropoietin level < 500 mU/mL

III. CONTINUATION OF THERAPY

Note: Requirements regarding current hemoglobin level exclude values due to a recent transfusion.

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 who meet BOTH of the following criteria:
1. The intent of chemotherapy is non-curative
2. Current hemoglobin is < 11 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.

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

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

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. 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

PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>BRAND NAME</th>
<th>BELVIQ (lorcaserin)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(generic)</td>
<td>BELVIQ XR (lorcaserin) extended-release</td>
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**Status:** CVS Caremark Criteria  
**Type:** Initial Prior Authorization  
**Ref # 793-A**

**FDA-APPROVED INDICATIONS**
Belviq and Belviq XR are 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 comorbid condition (e.g., hypertension, dyslipidemia, type 2 diabetes)

**Limitations of Use:**
- The safety and efficacy of coadministration with other products intended for weight loss including prescription drugs (e.g., phentermine), over-the-counter drugs, and herbal preparations have not been established
- The effect on cardiovascular morbidity and mortality has not been established

**COVERAGE CRITERIA**
Belviq and Belviq XR will be covered with prior authorization when the following criteria are met:
- The patient has completed at least 3 months of therapy with the requested drug AND
  - The patient has lost at least 5 percent of baseline body weight or has continued to maintain their weight loss
- OR
- The requested medication 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. Belviq and Belviq XR are 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 comorbid condition (e.g., hypertension, dyslipidemia, type 2 diabetes). The safety and efficacy of coadministration of Belviq with other products intended for weight loss including prescription drugs (e.g., phentermine), over-the-counter drugs, and herbal preparations have not been established. The effect of Belviq on cardiovascular morbidity and mortality has 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 ≥ 30 kg/m² or ≥ 27 kg/m² if other risk factors are present (e.g., hypertension, diabetes, dyslipidemia, sleep apnea, cardiovascular disease).4-6
The safety and efficacy of Belviq for chronic weight management in conjunction with reduced caloric intake and increased physical activity were evaluated in 3 randomized, double-blind, placebo-controlled trials with durations ranging from 52 to 104 weeks. Patients receiving lorcaserin 10 mg either once or twice daily had significantly more weight loss than patients receiving placebo, and those receiving lorcaserin twice daily experienced greater weight loss than those receiving lorcaserin once daily in the 52-week randomized, double-blind Behavioral Modification and Lorcaserin for Overweight and Obesity Management (BLOOM) study. In the 2-year, randomized, double-blind BLOOM trial, patients receiving lorcaserin 10 mg twice daily lost significantly more weight over 1 year and were more likely to maintain that weight loss during the second year compared with patients receiving placebo.

For renewal after 12 weeks of therapy, the patient must have lost at least 5% of baseline body weight. It is recommended that therapy be discontinued after 12 weeks if the patient did 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.

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 re-reviewed with the patient and lack of long-term data is acknowledged.

REFERENCES
CRITERIA FOR APPROVAL

1. Has the patient completed at least 3 months of therapy with the requested drug?  
   [If no, then skip to question 3.]  
   **Yes**  **No**

2. Did the patient lose at least 5 percent of baseline body weight or has the patient continued to maintain their weight loss?  
   [No further questions required.]  
   **Yes**  **No**

3. 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 5.]  
   **Yes**  **No**

4. 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**

5. 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>12 Months</th>
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### Mapping Instructions

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<th>DENIAL REASONS – DO NOT USE FOR MEDICARE PART D</th>
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</thead>
<tbody>
<tr>
<td>1.</td>
<td>Go to 2</td>
<td>Go to 3</td>
</tr>
</tbody>
</table>
| 2.  | Approve for 12 months. | Deny | 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  
you have risk factors  
Your use of this drug does not meet the requirements. This is based on the information we have. |
| 3.  | Go to 5 | Go to 4 | Your plan covers this drug when you will diet and exercise.  
Your use of this drug does not meet the requirement. This is based on the information we have. |
| 4.  | Go to 5 | Deny | Your plan covers this drug when you have lost at least 5 percent of your body weight or have continued to keep your weight loss off. Your use of this drug does not meet the requirement. This is based on the information we have. |
| 5.  | Approve for 3 months. | Deny | Your plan covers this drug when you will diet and exercise.  
Your use of this drug does not meet the requirement. This is based on the information we have. |
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.

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

B. Compendial Uses
   Prophylaxis of 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


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 Indications
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. CRITERIA FOR INITIAL APPROVAL

Acute lymphoblastic leukemia (ALL)
Authorization of 12 months may be granted for treatment of relapsed or refractory ALL when both of the following criteria are met:
A. Member has B-cell precursor ALL, AND
B. The tumor is CD22-positive as confirmed by testing or analysis to identify the CD22 protein on the surface of the B-cell.

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

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 24 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 24 months may be granted to members for the treatment of a first clinical episode of 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

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

2. bortezomib [package insert]. Lake Zurich, IL: Fresenius Kabi; November 2017
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
   Bosulif is indicated for the treatment of adult patients with
   1. Newly-diagnosed chronic phase Philadelphia chromosome-positive (Ph+) chronic myelogenous leukemia (CML)
   2. Chronic, accelerated, or blast phase Ph+ CML with resistance or intolerance to prior therapy.

B. Compendial Uses
   1. 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)

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

II. CRITERIA FOR INITIAL APPROVAL

Chronic Myelogenous Leukemia (CML)

Authorization of 12 months may be granted for members initiating treatment with Bosulif for CML when ALL of the following criteria are met:

   1. Diagnosis of CML was confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing
   2. Member meets criteria outlined in Section A, B, or C below

A. CML, Chronic Phase (CP-CML)

Authorization of 12 months may be granted for members initiating Bosulif for the treatment of CP-CML when ONE of the following criteria is met:

   1. Member has not received prior therapy with a tyrosine kinase inhibitor (TKI) (e.g., dasatinib, imatinib, nilotinib, ponatinib)
   2. Member has experienced resistance to prior therapy with a TKI (e.g., dasatinib, imatinib, nilotinib, ponatinib) AND results of mutational testing are negative for T315I mutation
   3. Member has experienced toxicity or intolerance to prior therapy with a TKI (e.g., dasatinib, imatinib, nilotinib, ponatinib)

B. CML, Accelerated Phase (AP-CML) or Blast Phase (BP-CML)

Authorization of 12 months may be granted for members initiating Bosulif for the treatment of AP- CML or BP-CML.
C. CML, Post-Hematopoietic Stem Cell Transplant (HSCT)
Authorization of 12 months may be granted for members who are initiating treatment with Bosulif and have received a HSCT for CML.

III. CONTINUATION OF THERAPY

Chronic Myelogenous Leukemia (CML)
Authorization of up to 12 months may be granted for members continuing treatment with Bosulif for CML when ALL of the following criteria are met:
1. Diagnosis of CML was confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing
2. Member meets ANY of the following criteria outlined in A or B:

A. CML, Chronic Phase (CP-CML)
Authorization of up to 12 months may be granted for members in CP-CML who have not received prior TKI therapy OR experienced resistance, toxicity, or intolerance to prior therapy with a TKI (e.g., dasatinib, imatinib, nilotinib, ponatinib) when member is receiving benefit from Bosulif therapy (i.e., achieved or maintained a cytogenic or molecular response to therapy)

B. CML, Accelerated Phase (AP-CML), Blast Phase (BP-CML), and Post-Hematopoietic Stem Cell Transplant (HSCT)
Authorization of 12 months may be granted for members continuing Bosulif for the treatment of AP-CML, BP-CML, and for members who have received a HSCT for CML.

IV. REFERENCES
PRIOR AUTHORIZATION CRITERIA

BRAND NAME: CIALIS 2.5 mg, 5 mg
(generic)
(tadalafil)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Quantity Limit

FDA-APPROVED INDICATIONS
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).

Limitations 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.

COVERAGE CRITERIA
Cialis 2.5 mg and 5 mg (tadalafil) will be covered with prior authorization when the following criteria are met:

- The patient does NOT require nitrate therapy on a regular or on an intermittent basis and will NOT be taking a guanylate cyclase (GC) stimulator, such as riociguat.

AND

- Cialis 2.5 mg or 5 mg is being prescribed for daily use for symptomatic benign prostatic hyperplasia (BPH) [Note: examples of signs and symptoms are incomplete emptying, weak stream, straining, urinary frequency, intermittency, urgency, or acute urinary retention.]

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. Cialis is indicated for the treatment of erectile dysfunction (ED), 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). However, the diagnosis of ED will not be included in these criteria for approval.

Cialis is intended for use in adult males only. Cialis is not indicated for use in newborns, children or women. Since BPH is typically a condition that occurs in older males, the Criteria for Approval does not specify this information related to the BPH diagnosis. Cialis was shown to potentiate the hypotensive effects of nitrates, and their administration to patients who are using nitrates, either regularly and/or intermittently, in any form is contraindicated. Do not use Cialis in patients who are using a guanylate cyclase (GC) stimulator, such as riociguat. PDE-5 inhibitors, including Cialis, may potentiate the hypotensive effects of GC stimulators.

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. Therapy decisions should be influenced by symptoms and prostate size. 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.4

The recommended dose of Cialis for once daily use for BPH is 5mg, taken at approximately the same time every day. For BPH, a starting dose of 2.5 mg is recommended for creatinine clearance 30 to 50 mL/min.1-3

The quantity for approval for Cialis (tadalafil) 2.5mg and 5mg will be 30 tablets per month.

REFERENCES

CRITERIA FOR APPROVAL

1. Does the patient require nitrate therapy on a regular or on an intermittent basis OR will the patient be taking a guanylate cyclase (GC) stimulator, such as riociguat?

   Yes  No

2. Is Cialis 2.5 mg or 5 mg being prescribed for daily use for symptomatic benign prostatic hyperplasia (BPH)?
   [Note: examples of signs and symptoms are incomplete emptying, weak stream, straining, urinary frequency, intermittency, urgency, or acute urinary retention.]

   Yes  No

   * 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>
<tbody>
<tr>
<td>1.</td>
<td></td>
<td>Deny  Go to 2 Your plan does not cover this drug when you use nitrate drugs either daily or on occasion, or if you use a guanylate cyclase stimulator. Your use of this drug does not meet this requirement. This is based on the information we have.</td>
</tr>
<tr>
<td>2.</td>
<td></td>
<td>Approve, 36 months 30 tablets per 25 days* 90 tablets per 75 days* Deny Your plan covers this drug when you have benign prostatic hyperplasia (BPH). Your use of this drug does not meet this requirement. This is based on the information we have.</td>
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Guidelines for Approval

<table>
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<tr>
<td>Quantity for Approval</td>
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Set 1

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</tr>
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<td>2</td>
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</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

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

V. CONTINUATION OF THERAPY

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

VI. REFERENCES

# PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>BRAND NAME</th>
<th>(generic)</th>
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<tr>
<td></td>
<td>(buprenorphine sublingual tablets)</td>
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**Status:** CVS Caremark Criteria  
**Type:** Initial Prior Authorization  
**Ref #:** 780-C

## 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.

Under the Drug Addiction Treatment Act (DATA) codified at 21 U.S.C. 823(g), prescription use of this product in the treatment of opioid dependence is limited to physicians who meet certain qualifying requirements, and who have notified the Secretary of Health and Human Services (HHS) of their intent to prescribe this product for the treatment of opioid dependence and have been assigned a unique identification number that must be included on every prescription.

## COVERAGE CRITERIA

- Buprenorphine sublingual tablets will be covered with prior authorization when the following criteria are met:
  - The drug is being used as part of a complete program for the treatment of opioid dependence including ALL of the following: behavioral therapies (e.g., individual therapy, group counseling, family behavior therapy, cognitive behavioral therapy, motivational enhancement, motivational incentives); medical history, physical exam, and screening laboratory tests as needed (e.g., HIV and hepatitis C screening); diversion control protocols such as observed dosing, pill counts, testing for buprenorphine’s metabolite (nor-buprenorphine) random testing for heroin and other drugs of abuse; use of the Prescription Drug Monitoring Program (PDMP) if available in state  
  - The prescriber agrees not to prescribe other opioids and the patient agrees not to take other opioids while the patient is taking buprenorphine  
  - The patient is pregnant or breastfeeding  
  - Buprenorphine is being prescribed for induction therapy and/or subsequent maintenance therapy for opioid dependence treatment  
  - Buprenorphine is being prescribed for INDUCTION THERAPY for transition from opioid use to opioid dependence treatment

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. Buprenorphine sublingual tablet is indicated for the treatment of opioid dependence and is preferred for induction. Buprenorphine sublingual tablet should be used as part of a complete treatment plan to include counseling and psychosocial support. Under the Drug Addiction Treatment Act (DATA) codified at 21 U.S.C. 823(g), prescription use of this product in the treatment of opioid dependence is limited to physicians who meet certain qualifying requirements, and who have notified the Secretary of Health and Human Services (HHS) of their intent to prescribe this product for the treatment of opioid dependence and have been assigned a unique identification number that must be included on every prescription.1-3

Ideal candidates for opioid addiction treatment with buprenorphine are individuals who have been objectively diagnosed with opioid addiction, are willing to follow safety precautions for treatment, can be expected to comply with treatment, and...
have no contraindications to buprenorphine therapy, and who agree to buprenorphine treatment after a review of
treatment options.\textsuperscript{4} Physicians who use buprenorphine to treat opioid addiction must consider the entire process of
treatment. The Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction - A Treatment
Improvement Protocol guideline (TIP 40) indicates the importance of educating patients about substance use, associated
problems, and prevention of relapse. The guidelines further recommend that progress be reassessed periodically.\textsuperscript{5}
Patients must agree not to take other opioids while taking buprenorphine, and prescribers must agree not to prescribe
other opioids while the patient is taking buprenorphine. In some situations, the short-term use of opioid analgesia for pain
management may be appropriate (e.g., surgeries).

According to the American Society of Addiction Medicine (ASAM) National Practice Guidelines, patients on buprenorphine
containing opioid agonist therapy should receive a comprehensive assessment including physical examination and
screening for hepatitis and HIV prior to beginning medication treatment. Diversion control protocols should be used such as
observed dosing, recall visits with pill counts, random drug testing for illicit drugs such as heroin, and testing for
buprenorphine and its metabolite (nor-buprenorphine). Accessing Prescription Drug Monitoring Program (PDMP) data is
advisable to check for other medications that the patient may be receiving.\textsuperscript{7}

To improve outcomes, buprenorphine therapy is recommended to be combined with behavioral therapies. Research
shows that when treating opioid dependence, a combination of medication and behavioral therapies is the most effective.
Behavioral therapies help patients engage in the treatment process, modify their attitudes and behaviors related to drug
and alcohol abuse, and increase healthy life skills. These treatments can also enhance the effectiveness of medications
and help people stay in treatment longer. Treatment programs that combine pharmacological and behavioral therapy
services increase the likelihood of cessation relative to programs without these services. There are a number of treatment
strategies that can be used in combination with medications to successfully address opioid dependence. These include
individual therapy, group counseling, family behavior therapy, cognitive behavioral therapy, motivational enhancement,
and motivational incentives.\textsuperscript{8}

There are three phases of maintenance treatment with buprenorphine for opioid addiction: Induction (usual duration is
approximately one week or less), Stabilization (usual duration approximately one to two months), and Maintenance.
Maintenance is the longest period that a patient is on buprenorphine. Maintenance can be relatively short-term (less than
twelve months) or a lifetime process. Data suggest that longer duration of medication treatment is associated with less
illicit drug use and fewer complications.\textsuperscript{5}

For non-pregnant patients, induction may be carried out using either buprenorphine/naloxone or buprenorphine depending
on the prescribing physician’s judgment.\textsuperscript{4,5} When the buprenorphine monotherapy formulation is used for induction, it is
recommended that it be used for no more than 2 days before switching to the buprenorphine/naloxone combination
formulation. Buprenorphine/naloxone is the preferred medication for maintenance treatment due to the presence of
naloxone in the formulation, which is intended to deter intravenous drug abuse by persons dependent on other opiates.\textsuperscript{5}

According to the TIP 40 guidelines, multiple previous attempts at detoxification which were followed by relapse to opioid
use are not a contraindication to maintenance with buprenorphine. Rather, such a history is a strong indication for
maintenance treatment with pharmacotherapy.\textsuperscript{5} In addition, the Centers for Substance Abuse Treatment (CSAT) TIP 43
guidelines recommend for patients who were unsuccessful at attempted medication tapering should be counseled that a
return to medication maintenance is more appropriate for some patients and does not represent treatment failure.\textsuperscript{6} For
induction, the dosage of buprenorphine should be individualized based on the type and degree of opioid dependence and
the timing of last use. For maintenance, the typical dosing range of buprenorphine is 4 to 24 mg once daily. Doses higher
than this have not been demonstrated to provide any clinical advantage.\textsuperscript{1-3} Non-pregnant patients undergoing induction
will be approved for 21 tablets every 3 months. Typical induction lasts 1 to 3 days and rarely over 7 days. This quantity
and duration of approval will allow the patient to have 7 days of induction therapy every 3 months. If there is further need
for induction, a buprenorphine combination product may be used. Setting a limit regarding the number of reauthorizations
is beyond the scope of this program and the decision to request reauthorization will be left at the discretion of prescribers.

Methadone is currently the standard of care in the United States for the treatment of opioid addiction in pregnant women.
Pregnant women presenting for treatment of opioid addiction should be referred to specialized services in methadone
maintenance treatment programs. If such specialized services are refused by a patient or are unavailable in the
community, maintenance treatment with the buprenorphine monotherapy formulation may be considered as an
alternative. Despite the fact that naloxone is classified by the FDA as a Pregnancy Category B drug (buprenorphine has
been classified by the FDA as a Pregnancy Category C drug), it should be used with caution in pregnant women who are addicted to opioids. Because both mother and fetus will be dependent on the opioids used by the mother, administration of naloxone could precipitate withdrawal in both. Thus, if it is determined that buprenorphine is the only acceptable option for the treatment of a pregnant woman, and she understands the issues and risks, then she should be treated with buprenorphine monotherapy so as not to risk fetal exposure to naloxone.5 Pregnant patients will be approved for 3 tablets per day for 10 months.

Mothers receiving buprenorphine monoproduct for the treatment of opioid use disorders should be encouraged to breastfeed. Naltrexone is not recommended for use during breastfeeding. In a study of buprenorphine and breastfeeding, it was shown that the amount of buprenorphine metabolites secreted in breast milk are so low that they pose little risk to breastfeeding infants. Breastfeeding patients will be approved for 12 months.

REFERENCES


Written by: UM Development (JH)
Date Written: 07/2003
Revised: (NB) 02/2005, 02/2006; (SE) 03/2009, 10/2009 (clarification); (CT) 12/2009; (KD) 04/2010 (added pregnancy information and Suboxone for induction); (SE) 07/2010 (added renewal criteria regarding use of other opioids/urine drug screen/changed duration of approval) 12-2009 (3), 07/2010 (added in QL question) 12-2009 (4), 09-2010 (removed QL and related question) 12-2009 (4); (CY) 03/2011 (added QL), 06/2011, 03/2012 (removed Suboxone, made separate document), 12/2012; (SE) 05/2013 (created commercial version), (SE) 09/2013; (CF) 09/2014, 05/2015 (added denial reasons), 09/2015; (CF/GB) 08/2016; (CF/JH) 01/2017 (no clinical changes), 04/2017 (added breastfeeding, clarified complete program question)

CRITERIA FOR APPROVAL

1  Is the drug being used as part of a complete program for the treatment of opioid dependence including ALL of the following: A) Behavioral therapies (e.g., individual therapy, group counseling, family behavior therapy, cognitive behavioral therapy, motivational enhancement, motivational incentives), B) Medical history, physical exam, and screening laboratory tests as needed (e.g., HIV and hepatitis C screening), C) Diversion control protocols such as observed dosing, pill counts, testing for buprenorphine’s metabolite (nor-buprenorphine), D) Random testing for heroin and other
drugs of abuse, E) Use of the Prescription Drug Monitoring Program (PDMP) if available in state?

2 Does the prescriber agree not to prescribe other opioids AND does the patient agree not to take other opioids while the patient is taking buprenorphine? Yes No

3 Is the patient pregnant or breastfeeding? Yes No
[If no, then skip to question 6.]

4 Is buprenorphine being prescribed for induction therapy and/or subsequent maintenance therapy for opioid dependence treatment? Yes No

5 Does the patient require use of MORE than 90 tablets per month? Yes No
[No further questions.]
[Tech Note: If yes, then deny and enter a partial approval for 90 tablets per month of buprenorphine.]

6 Is buprenorphine being prescribed for INDUCTION THERAPY for transition from opioid use to opioid dependence treatment? Yes No

7 Does the patient require use of MORE than 21 tablets? Yes No
[Tech Note: If yes, then deny and enter a partial approval for 21 tablets per 75 days of buprenorphine.]
<table>
<thead>
<tr>
<th></th>
<th></th>
<th>based on the information we have.</th>
</tr>
</thead>
</table>
| 5. | Deny | Approve, 10 months 90 tablets per 25 days*  
270 tablets per 75 days* |
|   |   | You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 90 tablets per month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers. Your request for additional quantities of the requested drug and strength has been denied. |
| 6. | Go to 7 | Deny |
|   |   | Your plan covers this drug when you are using buprenorphine to start addiction treatment. Your use of this drug does not meet the requirement. This is based on the information we have. |
| 7. | Deny | Approve, 3 months 21 tablets per 75 days* |
|   |   | You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 21 tablets of the requested drug and strength. You have been approved for the maximum quantity that your plan covers. 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

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\(^1\)
   Advanced renal cell carcinoma (RCC)

B. Compendial Uses\(^2\)
   1. Relapse or stage IV kidney cancer
   2. Non-small cell lung cancer

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

II. CRITERIA FOR INITIAL APPROVAL

A. Renal Cell Carcinoma\(^1\)\(^3\)
   Authorization of 12 months may be granted for treatment of relapsed, unresectable, or metastatic renal cell carcinoma.

B. Non-small Cell Lung Cancer\(^2\)
   Authorization of 12 months may be granted for treatment of non-small cell lung 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

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 12 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
3. Member is 18 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

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

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

A. 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

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 chronic 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
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

PRIOR AUTHORIZATION CRITERIA

<table>
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<td>CVS Caremark Criteria</td>
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<td>Initial Prior Authorization</td>
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<tr>
<td>Ref #:</td>
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</table>

**COVERAGE CRITERIA**

Compounded drug products will be covered with prior authorization when the following criteria are met:

- The request is for injectable or intravenous use [e.g., anti-infective/antibiotic, heparin, total parenteral nutrition (TPN), hydroxyprogesterone, leuprolide acetate for infertility in a patient unable to utilize the FDA-approved commercially available product (1mg per 0.2mL kit)], or pyrimethamine

*OR*

- Each of the active ingredients in the compound are FDA-approved drugs
- Each of the active ingredients in the compound are used for an FDA-approved indication for which the compound is being prescribed
- The compound route of administration (ROA) is the same as the FDA-approved route of administration for each active ingredient
- The dosage or concentration of each active ingredient in the compound is equal to or below the FDA-approved dosage or concentration
- The request is not for a topical compound or a topical compound kit (e.g., cream, gel, lotion, ointment)
- The compound is not intended for anti-aging or cosmetic use, or is not a compound kit, or does not contain any of the following ingredients: bulk powder (e.g., estriol, ketamine, naltrexone, testosterone), or dietary supplements [e.g., aloe vera, citrulline, coenzyme Q10, DHEA (dehydroepiandrosterone), hyaluronic acid, lipoic acid, methylcobalamin, resveratrol, valine, vanadium]
- The request is not for a hormone therapy compound for menopause or for androgen decline due to aging, (e.g., testosterone, estrogen, progestin, bioidentical hormone)
- Coverage is provided for additional fills of the compounded drug if patient needs more than 1 fill per month (necessity may include continuation of antibiotic therapy, stability is less than a month, dose adjustment)

**AND**

- There is a current supply shortage of the commercially manufactured product
  *OR*
  - The patient has a medical need for a dosage form or dosage strength that is not available commercially or manufactured
    *OR*
    - The patient had an intolerance or contraindication to the commercially manufactured product (e.g., allergen, adverse effects to inactive ingredients)
      *OR*
      - The commercial product has been discontinued by the pharmaceutical manufacturer for reasons other than lack of safety or effectiveness
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.

Products for injectable or intravenous use [e.g., anti-infective/antibiotic, heparin, total parenteral nutrition (TPN), hydroxyprogesterone, leuprolide acetate for infertility in a patient unable to utilize the FDA-approved commercially available product (1mg per 0.2mL kit)], or pyrimethamine are covered.

Topical compounds and topical compound kits (e.g. cream, gel, lotion, ointment) are not covered.

Compounds for anti-aging or cosmetic use, or compound kits, or compounds that contain a bulk powder (e.g., estriol, ketamine, naltrexone, testosterone) or dietary supplements [e.g., aloe vera, citrulline, coenzyme Q10, DHEA (dehydroepiandrosterone), hyaluronic acid, lipoic acid, methylcobalamin, resveratrol, valine, vanadium] are not covered.

Hormone therapy compounds (e.g. testosterone, estrogens, progestins, bioidentical hormones) for menopause or for androgen decline due to aging are not covered. FDA is not aware of any credible scientific evidence to support claims made regarding the safety and effectiveness of compounded bio-identical hormone replacement therapy drugs. In addition, FDA has not approved any drug containing the hormone estriol. There are FDA-approved brand-name and generic manufactured menopausal hormone therapy and hormone replacement therapy products that are available in a variety of strengths and dosage forms (e.g., tablet, patch, gel, injectable, vaginal cream).

Compounding does not include mixing or reconstituting commercial products in accordance with the manufacturer's instructions or the product's approved labeling. Bulk ingredients are not FDA-approved products. Compounded drugs are not FDA-approved. The safety or effectiveness of compounded drugs are not verified by the FDA. Compounded drugs also lack an FDA finding of manufacturing quality before such drugs are marketed. The FDA does not allow the marketing of compounding drugs that were withdrawn or removed from the market due to lack of safety or effectiveness; or compounding drug products that are commercially available in the marketplace or that are essentially copies of commercially available FDA-approved drug products.

Pharmaceutical compounding is the combining, mixing, or altering of ingredients to create a customized medication that is not otherwise commercially available and is medically necessary for an individual patient in response to a licensed practitioner's prescription. There may be situations where a compound prescription is necessary due to special patient needs for customized therapies. Health needs that commercially available prescription medicines cannot meet may include:

- drug shortages, the need to access drugs or dosage forms withdrawn from the market, or medication is discontinued by or generally unavailable from pharmaceutical companies
- patient is allergic to certain preservatives, dyes or binders in commercially available medications (e.g., allergen-free medications)
- treatment requires tailored dosage strengths for patients with unique needs (e.g., an infant, non-standard doses, and parenteral nutrition)
- patient cannot ingest the medication in its commercially available form and the medication can be prepared in another form that the patient can ingest.

There may be a need to fill the compound prescription more than once per month (necessity may include continuation of antibiotic therapy, stability of water-containing formulation is less than a month, dose adjustment).
REFERENCES


<table>
<thead>
<tr>
<th>CRITERIA FOR APPROVAL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1</strong></td>
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<td><strong>9</strong></td>
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<td><strong>10</strong></td>
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</table>
11 Has the patient had an intolerance or contra indication to the commercially manufactured product (e.g., allergen, adverse effects to inactive ingredients)?
[If yes, then skip to question 13.]

<table>
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12 Has the commercial product been discontinued by the pharmaceutical manufacturer for reasons other than lack of safety or effectiveness?

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13 Does the patient need more than 1 fill per month of the compounded drug (necessity may include continuation of antibiotic therapy, stability is less than a month, dose adjustment)?

<table>
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[Tech note: for Commercial clients: All compound claims $5000 and over must be reviewed by a pharmacist prior to approval. Select the appropriate RPh denial close option to send to RPh for review.]

### Mapping Instructions

<table>
<thead>
<tr>
<th>Yes</th>
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</table>

1. **Deny**
   - Go to 2
   - Your plan does not cover this compounded drug when it is for topical use. Your use of this drug does not meet the requirement. This is based on the information we have.

2. **Approve, 3 months, remove Fill Limit**
   - Go to 3

3. **Deny**
   - Go to 4
   - Your plan does not cover this compounded drug when you use the drug for anti-aging or cosmetic reasons. Your plan does not cover this drug if it is a compound kit. Your plan also does not cover the compounded drug when it contains any of the following:
     - Bulk powder (examples are estriol, ketamine, naltrexone, testosterone)
     - Dietary supplements [examples are aloe vera, citrulline, coenzyme Q10, DHEA (dehydroepiandrosterone), hyaluronic acid, lipoic acid, methylcobalamin, resveratrol, valine, vanadium]
   - Your use of this drug does not meet the requirements. This is based on the information we have.

4. **Deny**
   - Go to 5
   - Your plan does not cover this compounded drug when you meet all of these conditions:
     - You use the drug as hormone therapy
     - You use the drug for menopause or androgen decline due to aging
   - Your use of this drug does not meet the requirements. This is based on the information we have.

5. Go to 6
   - Deny
   - Your plan covers this drug when each of the active ingredients is an FDA-approved drug. Your use of this drug does not meet the requirement. This is based on the information we have.

6. Go to 7
   - Deny
   - Your plan covers this drug when each of the active ingredients is FDA-approved for the condition being treated. Your use of this drug does not meet the requirement. This is based on the information we have.

7. Go to 8
   - Deny
   - Your plan covers this drug when you take or use it by the same route as the FDA-approved route for each active ingredient. Your use of this drug does not meet the requirement. This is based on the information we have.
<table>
<thead>
<tr>
<th>8.</th>
<th>Go to 9</th>
<th>Deny</th>
<th>Your plan covers this drug when the dosage is at or below the FDA-approved dosage for each active ingredient. Your use of this drug does not meet the requirement. This is based on the information we have.</th>
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</thead>
<tbody>
<tr>
<td>9.</td>
<td>Go to 13</td>
<td>Go to 10</td>
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<tr>
<td>11.</td>
<td>Go to 13</td>
<td>Go to 12</td>
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</tbody>
</table>
| 12. | Go to 13 | Deny | Your plan covers this compounded drug when one of these conditions applies:  
- There is a supply shortage of the manufactured drug  
- You need a form or strength of the manufactured drug that is not available  
- You tried the manufactured drug and it either did not work for you or you cannot take it  
- You have a contraindication to the manufactured drug  
- The drug manufacturer stopped making the drug for reasons other than the lack of safety or the drug not working  
Your use of this drug does not meet the requirement. This is based on the information we have. |
| 13. | Approve, 3 months, remove Fill Limit | Approve, 3 months | |
**PRIOR AUTHORIZATION CRITERIA**

**BRAND NAME**
CONTRAVE (generic) (naltrexone HCl and bupropion HCl extended release)

**Status:** CVS Caremark Criteria  
**Type:** Initial Prior Authorization  
**Ref # 1190-A**

**FDA-APPROVED INDICATIONS**
Contrave 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 comorbid condition (e.g., hypertension, dyslipidemia, type 2 diabetes)

**Limitations of Use:**
- The effect of Contrave on cardiovascular morbidity and mortality has not been established.
- The safety and effectiveness of Contrave 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**
- Contrave will be covered with initial prior authorization for 4 months when the following criteria are met:
  - The requested medication 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.

- Contrave will be covered with renewal prior authorization for 36 months when the following criteria are met:
  - The patient has completed at least 4 months of Contrave therapy and lost at least 5 percent of baseline body weight or has continued to maintain their weight loss.

**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. Contrave 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 comorbid condition (e.g., hypertension, dyslipidemia, type 2 diabetes). The safety and efficacy of coadministration of Contrave with other products intended for weight loss including prescription drugs, over-the-counter drugs, and herbal preparations have not been established. The effect of Contrave on cardiovascular morbidity and mortality has 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 ≥ 30 kg/m² or ≥ 27 kg/m² if other risk factors are present (e.g., hypertension, diabetes, dyslipidemia, sleep apnea, cardiovascular disease).4-6

Contrave will be approved initially for 4 months to allow for dose escalation to the maintenance dosage and 12 weeks of maintenance therapy. For renewal after 4 months of Contrave therapy, the patient must have lost at least 5% of baseline body weight. If a patient has not lost at least 5% of baseline body weight, Contrave should be discontinued as it is unlikely that the patient will 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 re-reviewed with the patient and lack of long-term data is acknowledged.4-6

REFERENCES

Written by: UM Development (PL)
Date Written: 09/2014
Revised: (MS) 07/2015, 12/2015 (updated Q6 to make trade compatible); (SE) 01/2016 (Added guidelines for approval grid); (MS) 07/2016 (removed safety question)
Reviewed: Medical Affairs (DNC) 09/2014; (MM) 07/2015

CRITERIA FOR APPROVAL

1. Has the patient completed at least 4 months of therapy with the requested drug? Yes No
   [If no, then skip to question 3.]

2. Did the patient lose at least 5 percent of baseline body weight or has the patient continued to maintain their weight loss? Yes No
   [No further questions required.]

3. Does the patient have a body mass index (BMI) greater than or equal to 30 kg per square meter? Yes No
   [If yes, then skip to question 5.]

4. 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

5. Will the requested medication be used with a reduced calorie diet and increased physical activity? Yes No
### Guidelines for Approval

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<thead>
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<th>Duration of Approval</th>
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### Mapping Instructions

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</table>
SPECIALTY GUIDELINE MANAGEMENT

COPAXONE (glatiramer acetate)
GLATOPA (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.

FDA-Approved Indication: Copaxone and Glatopa are indicated for the treatment of patients with relapsing forms of multiple sclerosis.

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 24 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 24 months may be granted to members for the treatment of a first clinical episode of 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

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

1. Authorization of 24 months may be granted for members who are 18 years of age or older who have received Cosentyx, Otezla, or any other biologic DMARD indicated for the treatment of moderate to severe plaque psoriasis in a paid claim through a pharmacy or medical benefit in the previous 120 days of the initial request for Cosentyx.

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 A).
      iii. Member has severe psoriasis that warrants a biologic DMARD as first-line therapy.

B. Active psoriatic arthritis (PsA)

1. Authorization of 24 months may be granted for members who are 18 years of age or older and who have received Cosentyx, Stelara or Otezla in a paid claim through a pharmacy or medical benefit in the previous 120 days of the initial request for Cosentyx.

2. Authorization of 24 months may be granted for treatment of active PsA in members 18 years of age or older when any of the following criteria is met:
   a. Member has had an inadequate response to at least a 3-month trial of at least one TNF inhibitor indicated for PsA (see Appendix B).
   b. Member has experienced an intolerance or adverse event to a trial of at least one TNF inhibitor indicated for PsA.
   c. All TNF inhibitors indicated for PsA are not appropriate for the member (e.g., due to comorbidities or a history of infections).
C. Active ankylosing spondylitis (AS)
   1. Authorization of 24 months may be granted for members who are 18 years of age or older and who have received Cosentyx or any other biologic DMARD indicated for active ankylosing spondylitis in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Cosentyx.
   2. Authorizations of 24 months may be granted for treatment of active AS 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) over a 4-week period in total at maximum recommended or tolerated anti-inflammatory dose.
      b. Member has an intolerance and/or contraindication to two or more NSAIDs (see Appendix C).

III. CONTINUATION OF THERAPY

   A. For plaque psoriasis:
      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 Cosentyx as evidenced by low disease activity or improvement in signs and symptoms of the condition.

   B. For psoriatic arthritis and ankylosing spondylitis:
      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) in a paid claim through a pharmacy or medical benefit in the previous 120 days of the continuation request are exempt from requirements related to TB screening in this Policy.

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 (male or female)
   6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

Appendix B: TNF Inhibitors Indicated for Psoriatic Arthritis
   1. Cimzia® (certolizumab pegol)
   2. Enbrel® (etanercept)
   3. Humira® (adalimumab)
   4. Remicade® (infliximab)
5. Simponi® (golimumab)

Appendix C: 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
PRIOR AUTHORIZATION CRITERIA

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<tr>
<td>MDC-1</td>
<td>Ref # 351-A</td>
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FDA-APPROVED INDICATIONS
Differin Gel 0.1% and Cream are indicated for the topical treatment of acne vulgaris.

Differin Gel 0.3% and Lotion are indicated for the topical treatment of acne vulgaris in patients 12 years of age and older.

COVERAGE CRITERIA
Differin will be covered with prior authorization when the following criteria are met:
- The patient has a diagnosis of acne vulgaris

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. Differin is indicated for the topical treatment of acne vulgaris. The criteria do not provide for cosmetic uses of this drug.

The safety and effectiveness of Differin in pediatric patients below the age of 12 have not been established.

The guidelines state that topical therapy is a standard of care in acne treatment. 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.7,8

REFERENCES
2. Differin Gel 0.1% [package insert]. Fort Worth, TX: Galderma Laboratories, L.P.; April 2011.
3. Differin Gel 0.3% [package insert]. Fort Worth, TX: Galderma Laboratories, L.P.; December 2013.
4. Differin Lotion 0.1% [package insert]. Fort Worth, TX: Galderma Laboratories, L.P.; December 2013.

Written by: UM Development (LS)
# CRITERIA FOR APPROVAL

<table>
<thead>
<tr>
<th>1</th>
<th>Does the patient have the diagnosis of acne vulgaris?</th>
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## Mapping Instructions

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<td><strong>1.</strong> Approve, 36 Months</td>
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**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**

Your plan covers this drug when you have acne vulgaris. Your use of this drug does not meet the requirements. This is based on the information we have.
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\(^1,2\)
   2. Conversion of AF/AFI to normal sinus rhythm\(^1,2\)

B. Compendial Uses
   1. Supraventricular tachycardia\(^3,4,6\)
   2. Ventricular tachyarrhythmia\(^3-5\)

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

II. CRITERIA FOR APPROVAL

1. Atrial Flutter/Atrial Fibrillation
   Authorization of 24 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 24 months may be granted for the treatment and prevention of supraventricular tachycardia.

3. Ventricular Tachyarrhythmia
   Authorization of 24 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


4. Clinical Consult. CVS Caremark Clinical Program Review: Focus on Cardiovascular Disease Programs; September 2012.

5. Clinical Consult. CVS Caremark Clinical Program Review: Focus on Cardiovascular Disease Programs; October 2010.

QUANTITY LIMIT CRITERIA

<table>
<thead>
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<td>(generic)</td>
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</tr>
<tr>
<td></td>
<td>MARINOL (dronabinol)</td>
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<tr>
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<td>SYNDROS (dronabinol)oral solution</td>
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Status: CVS Caremark Criteria
Type: Quantity Limit
Ref # 137-H

FDA-APPROVED INDICATIONS
Marinol and Syndros are indicated for the treatment of:
- anorexia associated with weight loss in patients with AIDS
- nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments.

RATIONALE

Appetite stimulation:
Initially, 2.5 mg dronabinol should be administered orally twice daily before lunch and supper. For patients unable to tolerate this 5 mg per day dosage of dronabinol, the dosage can be reduced to 2.5 mg per day, administered as a single dose in the evening or at bedtime. If clinically indicated and in the absence of significant adverse effects, the dosage may be gradually increased to a maximum of 20 mg per day, administered in divided oral doses. Caution should be exercised in escalating the dosage of dronabinol because of the increased frequency of dose-related adverse experiences at higher dosages.

Antiemetic:
Dronabinol is best administered as an initial dose of 5 mg per square meter, given one to three hours prior to the administration of chemotherapy, then every two to four hours after chemotherapy is given, for a total of four to six doses per day. Should the 5-mg per square meter dose prove to be ineffective, and in the absence of significant side effects, the dose may be escalated by 2.5 mg per square meter increments, to a maximum of 15 mg per square meter per dose. Caution should be exercised in dose escalation, however, as the incidence of disturbing psychiatric symptoms increases significantly at maximum dose.

The limit will accommodate the treatment of AIDS-associated weight loss as well as chemotherapy-related nausea and vomiting during a chemotherapy cycle at the recommended dosages.

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

REFERENCES
### LIMIT CRITERIA

Limits should accumulate across all drugs and strengths up to highest quantity listed depending on the order the claims are processed. Accumulation does not apply if limit is coded for daily dose.

<table>
<thead>
<tr>
<th>Drug</th>
<th>1 Month Limit*</th>
<th>3 Month Limit*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marinol 2.5 mg, 5 mg, 10 mg capsules</td>
<td>60 capsules /25 days</td>
<td>180 capsules /75 days</td>
</tr>
<tr>
<td>Syndros oral solution</td>
<td>120 mL/25 days</td>
<td>360 mL/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

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 Indication
Dupixent is indicated for the treatment of adult patients 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.

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

II. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a dermatologist or an allergist/immunologist.

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 4 months may be granted for treatment of moderate-to-severe atopic dermatitis in members 18 years of age or older when either of the following criteria is met:

1. Member has had an inadequate treatment response to a topical corticosteroid or a topical calcineurin inhibitor in the past 180 days.

2. The use of topical corticosteroids and topical calcineurin inhibitors is not advisable for the member (e.g., due to contraindications or prior intolerances).

IV. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for members 18 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 or improvement in signs and symptoms of atopic dermatitis (e.g., redness, itching, oozing/crusting).

V. REFERENCES


PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>ALPROSTADILS</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRAND NAME (generic)</td>
<td>CAVERJECT (alprostadil)</td>
</tr>
</tbody>
</table>

**Status:** CVS Caremark Criteria  
**Type:** Initial Prior Authorization with Quantity Limit  
Ref # 1044-C

FDA-APPROVED INDICATIONS

**Caverject**  
Caverject Impulse, Caverject Sterile Powder, and Caverject Injection are indicated for the treatment of erectile dysfunction due to neurogenic, vasculogenic, psychogenic, or mixed etiology. Intracavernosal 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

Caverject (alprostadil), Edex (alprostadil), and MUSE (alprostadil) will be covered with prior authorization when the following criteria are met:

- The patient does NOT have any of the following: A condition that may predispose to priapism, Anatomical deformation of the penis, A condition where sexual activity is inadvisable, Penile implants, or for MUSE only: sexual intercourse with a pregnant person UNLESS the couple uses a condom barrier
- The 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 intended for use in adult males only. They are not indicated for use in newborns, children or women. Alprostadil (e.g., Caverject, Edex, MUSE) should not be used in patients who have conditions that might predispose them to priapism, such as sickle cell anemia or trait, multiple myeloma, or leukemia; or, in patients with anatomical deformation of the penis, such as angulation, cavernosal fibrosis, or Peyronie's disease. Patients with penile implants should not be treated with alprostadil. Alprostadil should not be used in men for whom sexual activity is inadvisable.1-6 MUSE should not be used for sexual intercourse with a pregnant woman unless the couple uses a condom barrier.4-6

According to the American Urological Association (AUA) Guideline on the Management of Erectile Dysfunction and the American Association of Clinical Endocrinologists (AACE), the management of erectile dysfunction begins with the identification of comorbidities and psychosexual dysfunctions; which should be appropriately treated.7 The dose of alprostadil should be individualized for each patient by careful titration under supervision by the physician.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. In the 2010 study by Eisenberg, et al., men and women between the ages of 25 and 45 have sex a mean 5.7 and 6.4 times per month, respectively.8 The 2007 Lindau, et al. study 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. In many of the drug clinical studies, patients were required to have a minimum amount of attempts or the frequency was restricted. 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
5. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.;

CRITERIA FOR APPROVAL

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Does the patient have any of the following: A) A condition that may predispose to priapism, B) Anatomical deformation of the penis, C) A condition where sexual activity is inadvisable, D) Penile implants, E) For MUSE only: sexual intercourse with a pregnant person UNLESS the couple uses a condom barrier?</td>
<td>Yes</td>
</tr>
<tr>
<td>2.</td>
<td>Is the drug being prescribed for erectile dysfunction in a patient that is 18 years of age or older?</td>
<td>Yes</td>
</tr>
</tbody>
</table>

DENIAL REASONS – DO NOT USE FOR MEDICARE PART D

1. Deny Go to 2  
   Your plan does not cover this drug when you have one of these conditions:
   - You have prolonged erections of your penis
   - You have a deformed penis
   - You were advised not to have sexual activity
   - You have a penile implant
   - If the request is for MUSE: You have sexual intercourse with a pregnant person without a condom
   Your use of this drug does not meet the requirements. This is based on the information we have.
2. **Approve for 36 months**
   (6 units/25 days* or 18 units/75 days*)

<table>
<thead>
<tr>
<th>Deny</th>
<th>Your plan covers this drug when you meet all of these conditions:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- You are 18 years of age or older</td>
</tr>
<tr>
<td></td>
<td>- You have erectile dysfunction</td>
</tr>
<tr>
<td></td>
<td>Your use of this drug does not meet the requirements. This is based on the information we have.</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.

<table>
<thead>
<tr>
<th>Guidelines for Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of Approval</td>
</tr>
<tr>
<td>Quantity for Approval</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>2</td>
<td>1</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

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
   2011;118:5767-5773.
   Ardinger HH, et al, editors. GeneReviews® [Internet]. Seattle, WA: University of Washington, Seattle;
   1993-2016.
PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>BRAND NAME (generic)</th>
<th>ELIDEL (pimecrolimus)</th>
</tr>
</thead>
</table>
| **Status**: CVS Caremark Criteria  
**Type**: Initial Prior Authorization | Ref # 759-A |

**FDA-APPROVED INDICATIONS**
Elidel is indicated as second-line therapy for the short-term and noncontinuous 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 Uses:**
- Psoriasis on the face, genitals, or skin folds.\(^2,3,5,6\)
- Vitiligo on the head or neck.\(^2,7,8\)

**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
  - The requested drug will be used on the face, body skin folds, genital area, armpit, or around the eyes
  - OR
  - 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 steroid)
  - OR
  - The patient is less than 2 years of age

**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. Elidel is indicated as second-line therapy for the short-term and noncontinuous 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.

In a Black Box Warning, the long-term safety of topical calcineurin inhibitors has not been established. Rare cases of malignancy (e.g., skin and lymphoma) have been reported in patients treated with topical calcineurin inhibitors, including Elidel (pimecrolimus) cream. Therefore, continuous long-term use of topical calcineurin inhibitors, including Elidel (pimecrolimus) cream, in any age group should be avoided, and application should be limited to areas of involvement with atopic dermatitis.\(^1\)

To initiate therapy, the patient must have the diagnosis of mild to moderate atopic dermatitis (eczema), psoriasis on the face, genitals, or skin folds, or vitiligo on the head or neck.\(^1-9\)
Topical corticosteroids are first-line treatment for atopic dermatitis flare-ups (see Table 1). Topical calcineurin inhibitors, such as Elidel (pimecrolimus), are considered second-line therapy. Elidel (pimecrolimus) is generally reserved for short-term or intermittent long-term therapy of atopic dermatitis, especially when there is concern that ongoing use of topical corticosteroids is causing adverse effects, such as atrophy. Because Elidel (pimecrolimus) does not lead to skin atrophy, it is particularly useful for areas of thinner skin on the face, neck, and skin folds.4 The request will be approved if the patient has experienced an inadequate treatment response, intolerance, or contraindication to at least one medium or higher potency topical steroid. However, if the area being treated is on the face, body skin folds, genital area, armpit, or around the eyes, Elidel (pimecrolimus) will be approved without requiring a trial of topical corticosteroid due to an increased risk of skin atrophy in thinner skinned areas.

<table>
<thead>
<tr>
<th>TABLE 1: EXAMPLES OF TOPICAL CORTICOSTEROIDS FOR TREATMENT OF ATOPIC DERMATITIS</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medium Potency</strong></td>
<td><strong>High Potency</strong></td>
</tr>
<tr>
<td>betamethasone valerate crm/ointment 0.1%/foam 0.12%</td>
<td>betamethasone dipropionate crm/ointment 0.05%</td>
</tr>
<tr>
<td>betamethasone dipropionate lotion 0.05%</td>
<td>betamethasone dipropionate augmented crm/ointment 0.05%</td>
</tr>
<tr>
<td>clocortolone pivalate crm 0.1%</td>
<td>desonide lotion, ointment 0.05%</td>
</tr>
<tr>
<td>desoximetasone crm 0.05%</td>
<td>desoximetasone crm/ointment/spray 0.25%/gel/ointment 0.05%</td>
</tr>
<tr>
<td>fluocinolone acetonide crm/oid/kit 0.025%</td>
<td>diflorasone diacetate crm (emollient base) 0.05%</td>
</tr>
<tr>
<td>flurandrenolide crm/ointment 0.05%</td>
<td>flurandrenolide tape 4mcg/cm²</td>
</tr>
</tbody>
</table>
| fluticasone propionate crm/ointment 0.05%/ointment 0.005% | fluticasone propionate crm/ointment 0.005%
| hydrocortisone butyrate oint/solution/cream 0.1% | Very High Potency |
| hydrocortisone probutate crm 0.1% | betamethasone dipropionate augmented ointment/gel 0.05%
| hydrocortisone valerate crm/ointment 0.2% | triamcinolone acetonide crm/ointment 0.5%
| mometasone furoate crm/ointment 0.1% | diflorasone diacetate ointment 0.05%
| prednicarbate crm/ointment 0.1% | mometasone furoate crm/ointment 0.1%
| triamcinolone acetonide aerosol solution 0.147 mg/g | flurbiprofen crm/ointment 0.1%
| triamcinolone acetonide crm/ointment/kit 0.1% | triamcinolone acetonide crm/ointment 0.025%
| triamcinolone acetonide ointment 0.05% | triamcinolone acetonide ointment 0.05%

Elidel (pimecrolimus) is not indicated for use in children less than 2 years of age.1 However, according to the American Academy of Dermatology Association (AAD) guidelines, for patients less than 2 years of age with mild to severe atopic dermatitis, off label use of 1% pimecrolimus ointment can be recommended.4 In a 5-year open label study, 2418 infants with atopic dermatitis were randomized to pimecrolimus with short term topical corticosteroids (TCS) for flares or topical corticosteroids. 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 atopic dermatitis 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.9 In a second group of 30 pediatric patients aged 3 to 23 months, 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 (pimecrolimus) for three weeks. In addition, a higher incidence of upper respiratory symptoms/infections was seen relative to the older age group.1 Taking safety and efficacy for the infant population into consideration, Elidel (pimecrolimus) will be considered for coverage for children less than 2 years of age with mild to moderate atopic dermatitis for short-term use (up to 3 months) without requiring a trial of a topical corticosteroid.
Based on the literature and compendia, Elidel (pimecrolimus) is an effective treatment of psoriasis on the face, genitals, or skin folds (intertriginous/inverse psoriasis). Topical corticosteroids are the cornerstone of treatment for the majority of patients with psoriasis, particularly those with limited disease. However, topical calcineurin inhibitors may be used in 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. In a double-blind, randomized, vehicle-controlled study of 57 patients with intertriginous psoriasis, 71% of the patients treated with pimecrolimus 1% cream were clear or almost clear after 8 weeks of twice-daily treatment as compared with 21% of patients treated with placebo. The study concluded that pimecrolimus 1% cream is an effective treatment for intertriginous psoriasis with a rapid onset of action and is safe and well-tolerated. Due to an increased risk of atrophy in thinner skinned areas, Elidel (pimecrolimus) will be considered for coverage to treat psoriasis on the face, genitals, or skin folds without requiring a trial of a topical corticosteroid.

Based on the literature and compendia, Elidel (pimecrolimus) is also an effective treatment of vitiligo on the head and neck. Vitiligo is an acquired cutaneous disorder of pigmentation, with an incidence of 0.5% to 2% worldwide. Topical corticosteroids and topical calcineurin inhibitors are now widely used as first-line treatment for limited forms of vitiligo. Beneficial effects of topical calcineurin inhibitors have been reported, particularly in areas where prolonged use of potent topical corticosteroids is contraindicated. Several randomized trials have been published, showing beneficial results mainly in the head and neck region, both in adults and children. Elidel (pimecrolimus) will be considered for coverage to treat vitiligo on the head and neck without requiring a trial of a topical corticosteroid.

REFERENCES


Written by: UM Development (KD)
Date Written: 04/2010
Revised: (MS) 02/2011, 03/2012 (new non-Medicare version), 03/2013, (CF) 03/2014, 03/2015, 01/2016 (updated question #4); (KM) 03/2016 (no clinical changes), 03/2017
Reviewed: Medical Affairs (KP) 04/2010, 02/2011, 03/2012, 03/2013; (LMS) 03/2014; (KRU) 03/2015; (DNC) 06/2015; (GAD) 03/2017

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.]
<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 Will the requested drug be used on the face, body skin folds, genital area, armpit, or around the eyes? [If yes, then no further questions.]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>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 steroid)? [If yes, then no further questions.]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 Is the patient less than 2 years of age? [No further questions.]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 Is the requested drug being prescribed for psoriasis on the face, genitals, or skin folds OR vitiligo on the head or neck?</td>
<td></td>
<td></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>Go to 5</td>
</tr>
<tr>
<td>2. Approve for 36 months</td>
<td>Go to 3</td>
</tr>
<tr>
<td>3. Approve for 36 months</td>
<td>Go to 4</td>
</tr>
<tr>
<td>4. Approve for 3 months</td>
<td>Deny</td>
</tr>
</tbody>
</table>

---

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

- You are using Elidel (pimecrolimus) on the face, body skin folds, genital area, armpits or around the eyes
- You tried a first line product (such as a medium or stronger steroid cream or ointment) and it did not work for you or you cannot use it
- You are less than 2 years of age

Your use of this drug does not meet the requirement. This is based on the information we have.

---

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>5. Approve for 36 months</td>
<td>Deny</td>
</tr>
</tbody>
</table>

---

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

- You have mild to moderate eczema and you are using Elidel (pimecrolimus) on the face, body skin folds, genital area, armpits or around the eyes
- You have mild to moderate eczema and you tried a first line product first and it did not work for you or you cannot use it
- You have mild to moderate eczema and you are less than 2 years of age
- You have psoriasis on your face, genitals, or skin folds
- You have vitiligo on your head or neck

Your use of this drug does not meet the requirement. This is based on the information we have.
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

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 received Enbrel or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) indicated for moderately to severely active rheumatoid arthritis in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Enbrel.

   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 received Enbrel or any other biologic DMARD indicated for active polyarticular juvenile idiopathic arthritis in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Enbrel.

   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 received Enbrel or any other biologic DMARD indicated for active ankylosing spondylitis in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Enbrel.

   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) over a 4-week period in total at maximum recommended or tolerated anti-inflammatory dose.
      b. Member has an intolerance and/or contraindication to two or more NSAIDs (see Appendix B).

E. Moderate to severe chronic plaque psoriasis
   1. Authorization of 24 months may be granted for members who have received Enbrel, Otezla, or any other biologic DMARD indicated for the treatment of moderate to severe chronic plaque psoriasis in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Enbrel.

   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 C).
         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.

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) in a paid claim through a pharmacy or medical benefit within the previous 120 days of the continuation request 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 (male or female)
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

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 (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

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
   Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naïve and have a fibrosis score ≥F1 or who failed prior treatment with peginterferon alfa (PEG-IFN) and ribavirin (RBV) with or without an HCV protease inhibitor (boceprevir, simeprevir or telaprevir).

2. Genotype 2 or 3 infection
   Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naïve and have a fibrosis score ≥F1 or who failed prior treatment with PEG-IFN and RBV.

3. 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-naïve and have a fibrosis score ≥F1 or who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor (boceprevir, simeprevir or telaprevir).

4. 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 or 4 infection and decompensated cirrhosis and documented anemia (baseline hemoglobin [Hgb] below 10 g/dL) or RBV ineligibility (see Section VI).

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 with compensated cirrhosis who failed prior treatment with an HCV NS5A inhibitor and do not have any NS5A inhibitor RAVs associated with velpatasvir resistance.

2. Genotype 2 infection
   Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with sofosbuvir and RBV.

3. Genotype 3 infection
   a. Authorization of up to 12 weeks total may be granted for members with the Y93H variant 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.

c. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with sofosbuvir and RBV.

4. 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 or 4 infection and decompensated cirrhosis who failed prior treatment with a sofosbuvir- or NS5A inhibitor-based 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.

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:
   A. Intolerance to RBV
   B. Pregnant female or male whose female partner is pregnant
   C. Hemoglobinopathy
   D. Coadministration with didanosine
   E. History of significant or unstable cardiac disease

V. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

EPOGEN, PROCRIT (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.

Limitations of Use:

1. Epoetin alfa has not been shown to improve quality of life, fatigue, or patient well-being.
2. Epoetin alfa is not indicated for use:
   • In patients with cancer receiving hormonal agents, biologic products, or radiotherapy, unless also receiving concomitant myelosuppressive chemotherapy.
   • In patients with cancer receiving myelosuppressive chemotherapy when the anticipated outcome is cure.
   • In patients scheduled for surgery who are willing to donate autologous blood.
   • In patients undergoing cardiac or vascular surgery.
   • As a substitute for RBC transfusions in patients who require immediate correction of anemia.

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

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.

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 who meet ALL of the following criteria:
1. The intent of chemotherapy is non-curative
2. Pretreatment hemoglobin < 10 g/dL

C. Anemia in MDS
Authorization of 12 weeks may be granted for members with pretreatment hemoglobin < 10 g/dL.

D. Reduction of Allogeneic Red Blood Cell Transfusion in Patients Undergoing Elective, Noncardiac, Nonvascular Surgery
Authorization of 12 weeks may be granted for members scheduled to have an elective, noncardiac, nonvascular surgery when the pretreatment hemoglobin is > 10 to ≤ 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.

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. Member has symptomatic anemia
2. Pretreatment hemoglobin < 10 g/dL
3. Pretreatment serum erythropoietin level < 500 mU/mL

III. CONTINUATION OF THERAPY

Note: Requirements regarding current hemoglobin level exclude values due to a recent transfusion.

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 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 who meet BOTH of the following criteria:
1. The intent of chemotherapy is non-curative
2. Current hemoglobin is < 11 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 ≤ 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 ≤ 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 ≤ 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 ≤ 12 g/dL.

IV. REFERENCES
PRIORITY 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 FOLFI R 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 panitumab.
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

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 12 months may be granted for treatment of idiopathic pulmonary fibrosis when all of the following criteria are met:
1. The member has undergone a diagnostic work-up which includes the following:
   a. The member does not have a known etiology for interstitial lung disease such as sarcoidosis, scleroderma, polymyositis/dermatomyositis, systemic lupus erythematosus, bronchiolitis obliterans organizing pneumonia, or drug toxicity AND
   i. The member has completed a high-resolution computed tomography (HRCT) study of the chest or surgical lung biopsy which reveals a result consistent with the usual interstitial pneumonia (UIP) pattern, OR
   ii. The member has completed an HRCT study of the chest which reveals a result consistent with the possible UIP pattern and the diagnosis is supported by surgical lung biopsy (SLB). If SLB has not been previously conducted, the diagnosis is supported by a multidisciplinary discussion between a radiologist and pulmonologist who are experienced in IPF.
2. Esbriet will not be used in combination with Ofev.

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 12 months when all of the following criteria are met:
1. The member is currently receiving treatment with Esbriet through health insurance (excludes obtainment as samples or via manufacturer’s patient assistance programs).
2. Esbriet will not be used in combination with Ofev.

IV. REFERENCES
STEP THERAPY CRITERIA with QUANTITY LIMIT

BRAND NAME
(generic)

EVZIO
(naloxone hydrochloride injection)

Status: CVS Caremark Criteria
Type: Initial Step Therapy with Quantity Limit;
Post Step Therapy Prior Authorization with Quantity Limit Ref # 1147-E

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.

INITIAL STEP THERAPY
If the patient has filled a prescription for at least a 1 day supply of buprenorphine, buprenorphine-naloxone, buprenorphine extended-release, fentanyl, fentanyl extended-release, hydrocodone extended-release, hydromorphone extended-release, meperidine, methadone, morphine extended-release, morphine/naltrexone extended-release, naltrexone, oxycodone extended-release, oxycodone/naloxone extended-release, oxymorphone extended-release, or tapentadol extended-release within the past 180 days under a prescription benefit administered by CVS Caremark, then Evzio 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 LIMIT CRITERIA

<table>
<thead>
<tr>
<th>Drug</th>
<th>1 Month Limit* and 3 Month Limit*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evzio (naloxone HCl injection)</td>
<td>2 cartons (4 auto-injectors) per 180 days</td>
</tr>
</tbody>
</table>

* The 1 month, 3 month, retail, and mail limits will be the same.

COVERAGE CRITERIA
Evzio will be covered with prior authorization when the following criteria are met:
- Evzio is being prescribed in the event that emergency treatment of opioid overdose may be needed
  - The patient previously had an overdose episode
    OR
  - The patient is taking any of the following for opioid dependence: buprenorphine, buprenorphine-naloxone, methadone, or naltrexone
    OR
  - The patient is, was, or will be, in an opioid dependence treatment program
    OR
o The patient is taking opioids, (e.g., buprenorphine, fentanyl, hydrocodone, hydromorphone, meperidine, methadone, morphine, oxycodone, oxymorphone, tapentadol), AND, alternative pain management therapies have been considered and the benefits of opioid therapy outweigh the risks of opioid overdose OR

o The patient is at risk for opioid overdose, misuse or abuse, either accidentally or intentionally AND

- If requesting more than 2 cartons (4 auto-injectors) per 6 months of Evzio, the patient requires more than 2 cartons due to
  - the type of opioid patient is taking (e.g., buprenorphine, pentazocine, long-acting/extended-release opioids) OR
  - the patient is living in area that has longer wait time for emergency medical assistance OR
  - the patient has had an overdose episode that required the use of naloxone or Evzio

Quantity Limits apply.

RATIONALE
The initial step prerequisite drugs will allow coverage of Evzio for patients who require any of the following within the past 180 days under a prescription benefit administered by CVS Caremark:

- Branded and generic drug products subject to the ER/LA opioid analgesic REMS i.e., buprenorphine extended-release, fentanyl extended-release, hydrocodone extended-release, hydromorphone extended-release, methadone, morphine extended-release, morphine/naltrexone extended-release, oxycodone extended-release, oxycodone/naloxone extended-release, oxymorphone extended-release, or tapentadol extended-release
- Drugs for detoxification, treatment, or maintenance therapy of opioid dependence/addiction i.e., buprenorphine oral, buprenorphine-naloxone, methadone, naltrexone
- Opioid drugs that have increased risk of toxicity/overdose i.e., fentanyl, meperidine

If the initial step therapy criteria are met, an initial quantity of 2 cartons (4 auto-injectors) per 180 days will be covered without prior authorization for the reasons that patients may need a repeat dose and may relapse within 6 months.

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. Evzio is 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.

Select medications that may place or identify patients who are at an increased risk of opioid overdose are included in the initial step prerequisite drugs. Medications used to treat opioid addiction in opioid treatment programs include methadone, buprenorphine, buprenorphine/naloxone, and naltrexone.6-7 Prolonged meperidine use may increase the risk of toxicity from the accumulation of the meperidine metabolite, normeperidine.3,4 The pharmacokinetic profile of fentanyl products results in clinical differences in absorption that could result in fatal overdose.3,4,11 ER/LA opioid analgesic drugs are subject to REMS that the FDA has determined was necessary to ensure that the benefits continue to outweigh their risks of adverse outcomes (addiction, unintentional overdose, and death).5,6,9,10

The World Health Organization (WHO) Substance Use Community Management of Opioid Overdose states that people taking prescribed opioids are at lower risk of overdose than people using unprescribed opioids. However, WHO also states that the high number of people receiving prescribed opioids in many countries mean that they constitute a significant proportion of opioid overdose deaths.6 The CDC Guideline for Prescribing Opioids for Chronic Pain recommends before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors
for opioid-related harms.\textsuperscript{9} Substance Abuse and Mental Health Services Administration (SAMHSA) Opioid Overdose Prevention Toolkit states that the risk of opioid overdose can be minimized through adherence to clinical practices, and even when sound medical indications have been established, physicians typically consider additional factors before deciding to prescribe an opioid analgesic.\textsuperscript{5} Therefore, in the event that an opioid overdose emergency treatment may be needed by the patient, Evzio may be covered if the patient is at risk for opioid overdose, misuse or abuse; or, the patient is taking opioids including those that are not listed as a prerequisite drug and the benefit of opioid therapy outweighs risk of respiratory or CNS depression.

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. Regulations specify two kinds of detoxification treatments with methadone (short-term <30 days and long-term 30 to 180 days), and patient selection for receiving maintenance therapy. 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. A warning sign of relapse is the illusion of feeling cured after a few weeks or months of abstinence.\textsuperscript{7} According to WHO, a reduction in tolerance, seen when opioid use is restarted after a period of abstinence, markedly increases the risk of an opioid overdose.\textsuperscript{8} Most patients resume opioid use within six months of opioid withdrawal and are at increased risk of overdose during the first weeks of treatment.\textsuperscript{6,8} Therefore, Evzio may be covered if the patient is taking a medication used to treat opioid addiction (buprenorphine, buprenorphine/naloxone, methadone, naltrexone), or, the patient is/was/will be in a dependence treatment program, or, the patient has a history of an overdose episode. In the event that opioid overdose emergency treatment may be needed and if the patient has used Evzio or requires additional quantities of Evzio within the initial 180 days, Evzio may be covered if criteria are met. The PA approved quantity will be an additional 2 cartons (4 auto-injectors) for a total of 4 cartons per 180 days.

Evzio automatically inserts the needle intramuscularly or subcutaneously and delivers 0.4mg or 2mg naloxone hydrochloride. If the desired response is not obtained after 2 or 3 minutes, another Evzio dose may be administered. If there is still no response and additional doses are available, additional Evzio 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 contains a single dose of naloxone. Evzio is supplied in a carton containing two auto-injectors.

The requirement for repeat doses of Evzio 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. The SAMHSA Opioid Overdose Prevention Toolkit states that most patients respond to naloxone generally within 3 to 5 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.\textsuperscript{6,8} Therefore, if the patient is living in an area of extended emergency response time or taking opioids that may require further dosing then a total of 4 cartons per 180 days may be covered.

\textbf{REFERENCES}\n


**CRITERIA FOR APPROVAL**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Is Evzio (naloxone) being prescribed in the event that emergency treatment of opioid overdose may be needed?</td>
</tr>
<tr>
<td>2</td>
<td>Has the patient previously had an overdose episode? [If yes, then skip to question 8.]</td>
</tr>
<tr>
<td>3</td>
<td>Is the patient taking any of the following for opioid dependence: buprenorphine, buprenorphine-naloxone, methadone, or naltrexone? [If yes, then skip to question 8.]</td>
</tr>
<tr>
<td>4</td>
<td>Was or is the patient, or will the patient be, in an opioid dependence treatment program? [If yes, then skip to question 8.]</td>
</tr>
<tr>
<td>5</td>
<td>Is the patient taking opioids (examples of immediate-release or extended-release opioids are buprenorphine, fentanyl, hydrocodone, hydromorphone, meperidine, methadone, morphine, oxycodone, oxymorphone, tapentadol)? [If no, then skip to question 7.]</td>
</tr>
<tr>
<td>6</td>
<td>Have alternative pain management therapies been considered and do the benefits of opioid therapy outweigh the risks of opioid overdose? [If yes, then skip to question 8.] [If no, then no further questions.]</td>
</tr>
<tr>
<td>7</td>
<td>Is the patient at risk for opioid overdose, misuse or abuse, either accidently or intentionally?</td>
</tr>
<tr>
<td>8</td>
<td>Does the patient require more than 2 cartons (4 auto-injectors) per 6 months of Evzio? Note: Coverage is provided for up to an initial quantity of 2 cartons per 6 months of Evzio. If higher quantities are needed, additional questions are required. [If no, then no further questions.]</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td>---</td>
<td>-----</td>
</tr>
<tr>
<td>1.</td>
<td>Go to 2</td>
</tr>
<tr>
<td>2.</td>
<td>Go to 8</td>
</tr>
<tr>
<td>3.</td>
<td>Go to 8</td>
</tr>
<tr>
<td>4.</td>
<td>Go to 8</td>
</tr>
<tr>
<td>5.</td>
<td>Go to 6</td>
</tr>
</tbody>
</table>
| 6. | Go to 8 | Deny | Your plan covers this drug when you meet any of these conditions:  
- You are at risk for opioid overdose, misuse or abuse  
- You had an overdose episode  
- You are taking buprenorphine, buprenorphine-naloxone, methadone, or naltrexone, for opioid dependence  
- You were, are, or will be, in an opioid dependence treatment program  
- You are taking an opioid, other pain therapies have been considered and the benefit of taking opioids outweighs the risk of overdose  
Your use of this drug does not meet the requirement. This is based on the information we have. |
| 7. | Go to 8 | Deny | Your plan covers this drug when you meet any of these conditions:  
- You are at risk for opioid overdose, misuse or abuse  
- You had an overdose episode  
- You are taking buprenorphine, buprenorphine-naloxone, methadone, or naltrexone, for opioid dependence  
- You were, are, or will be, in an opioid dependence treatment program  
- You are taking an opioid, other pain therapies have been considered and the benefit of taking opioids outweighs the risk of overdose  
Your use of this drug does not meet the requirement. This is based on the information we have. |
<p>| 8. | Go to 9 | Approve, 6 months, 2 cartons (4 auto-injectors) per 180 |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>days* per each PA request</td>
<td>No More Than 4 cartons total per 180 days</td>
</tr>
<tr>
<td>9.</td>
<td>Go to 10</td>
<td>Deny</td>
</tr>
<tr>
<td></td>
<td>Your plan covers this drug for more than 2 cartons (4 auto-injectors)/6 months when you meet any of these conditions:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- You are taking a certain type of opioid (examples are buprenorphine, pentazocine, long-acting/extended-release)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- You live in area that has longer wait time for emergency medical assistance</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- You had an overdose episode that required the use of naloxone or this drug</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>10.</td>
<td>Deny</td>
<td>Approve, 6 months, 4 cartons (8 auto-injectors) per 180 days*</td>
</tr>
<tr>
<td></td>
<td>No More Than 4 cartons total per 180 days</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 a total of 4 cartons (8 auto-injectors)/6 months of Evzio.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>You have been approved for the maximum quantity that your plan covers. Your request for additional quantities of the requested drug and strength has been denied.</td>
<td></td>
</tr>
</tbody>
</table>

* The 1 month, 3 month, retail, and mail limits will be the same.
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

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 are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Severe eosinophilic asthma
Authorization of 12 months may be granted for treatment of severe asthma with an eosinophilic phenotype when all of the following criteria are/is met:
A. Member is 12 years of age or older
B. Member has a baseline blood eosinophil count of at least 300 cells per microliter
C. Member has a history of severe asthma despite current treatment with both of the following medications at optimized doses:
   1. Inhaled corticosteroid
   2. Additional controller (long acting beta_2-agonist, leukotriene modifier, or sustained-release theophylline)

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for treatment of severe asthma with an eosinophilic phenotype 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, demonstrated by either:
   1. A reduction in the frequency and/or severity of symptoms and exacerbations
   2. A reduction in the daily maintenance oral corticosteroid dose

IV. REFERENCES

SPECIALTY GUIDELINE MANAGEMENT

GILENYA (fingolimod)
  fingolimod (generic)

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/fingolimod is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS) to reduce the frequency of clinical exacerbations and to delay the accumulation of physical disability.

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

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 24 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis.

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

FIRAZYR (icatibant)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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 are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Indefinite authorization may be granted for treatment of acute hereditary angioedema attacks in members 18 years of age or older 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


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.

A. FDA-Approved Indications
   1. Treatment of postmenopausal women with osteoporosis at high risk for fracture
   2. Increase of bone mass in men with primary or hypogonadal osteoporosis at high risk for fracture
   3. 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. CRITERIA FOR INITIAL APPROVAL

A. Osteoporosis in Postmenopausal Women
   Authorization of a lifetime total of 24 months may be granted to postmenopausal female members when ANY of the following criteria are met:
   1. Member has a history of fragility fractures
   2. Member has a pre-treatment T-score of < -2.5 OR member has osteopenia 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, or increased fall risk)
      b. Member has failed prior treatment with or is intolerant to previous osteoporosis therapy (i.e., oral bisphosphonates or injectable antiresorptive agents)

B. Primary or Hypogonadal Osteoporosis in Men
   Authorization of a lifetime total of 24 months 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 has a pre-treatment T-score of ≤ -2.5
   3. Member has osteopenia with a high pre-treatment FRAX fracture probability (See Appendix B)

C. Glucocorticoid-induced Osteoporosis
   Authorization of a lifetime total of 24 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 ≤ -2.5
      c. Member has osteopenia with a high pre-treatment FRAX fracture probability (See Appendix B)
III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria AND has received less than 24 months of total lifetime therapy with Forteo.1

IV. 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 < 30 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: http://www.shef.ac.uk/FRAX/tool.jsp

V. 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 patients with relapsing forms of multiple sclerosis (MS) to reduce the frequency of clinical exacerbations and to delay the accumulation of physical disability.

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

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 24 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis.

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

**BRAND NAME***
(generic)

<table>
<thead>
<tr>
<th>BRAND NAME*</th>
<th>(generic)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GRASTEK</strong></td>
<td>(timothy grass pollen allergen extract)</td>
</tr>
</tbody>
</table>

**Status:** CVS Caremark Criteria  
**Type:** Initial Prior Authorization  
**Ref #** 1133 -A  

*Drugs that are listed in the target drug box include both brand and generic and all dosages forms and strengths unless otherwise stated*

### FDA-APPROVED INDICATIONS

Grastek is an allergen extract indicated as immunotherapy for the treatment of grass pollen-induced allergic rhinitis with or without conjunctivitis confirmed by positive skin test or *in vitro* testing for pollen-specific IgE antibodies for Timothy grass or cross-reactive grass pollens. Grastek is approved for use in persons 5 through 65 years of age. Grastek is not indicated for the immediate relief of allergic symptoms.

### 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 grass pollen-induced allergic rhinitis, with or without conjunctivitis, confirmed by positive skin test or *in vitro* testing for pollen-specific IgE antibodies for timothy grass pollen grass allergen extract.
  
- The patient does not have any of the following: severe, unstable or uncontrolled asthma, history of any severe systemic allergic reaction or any severe local reaction to sublingual allergen immunotherapy, history of eosinophilic esophagitis, medical conditions that may reduce the ability of the patient to survive a serious allergic reaction or increase the risk of adverse reactions after epinephrine administration and is not on any medication(s) that can inhibit or potentiate the effect of epinephrine.
  
### 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.

Allergic rhinitis affects 20 to 40 percent of the population in the United States annually. Effective management of allergic rhinitis may require combinations of aggressive avoidance measures (e.g., avoidance of rhinitis triggers, limiting outdoor exposure when high pollen counts are present), medications, management of coexisting conditions, and/or allergen immunotherapy. A wide range of oral and intranasal pharmacologic treatments exists consisting of antihistamines, decongestants, corticosteroids, cromolyn, anticholinergics, anti-leukotriene agents, and nasal saline.

Grastek is an allergen extract indicated as immunotherapy for the treatment of grass pollen-induced allergic rhinitis with or without conjunctivitis confirmed by positive skin test or *in vitro* testing for pollen-specific IgE antibodies for Timothy grass or cross-reactive grass pollens. Grastek is approved for use in persons 5 through 65 years of age. Grastek is not indicated for the immediate relief of allergic symptoms.
Grastek may not be suitable for patients with certain medical conditions that may reduce the ability to survive a serious allergic reaction or increase the risk of adverse reactions after epinephrine administration. Examples of these medical conditions include but are not limited to: markedly compromised lung function (either chronic or acute), unstable angina, recent myocardial infarction, significant arrhythmia, and uncontrolled hypertension.

Grastek may not be suitable for patients who are taking medications that can potentiate or inhibit the effect of epinephrine. These medications include beta-adrenergic blockers, alpha-adrenergic blockers, ergot alkaloids, tricyclic antidepressants, levothyroxine sodium, monoamine oxidase inhibitors, the antihistamines chlorpheniramine and diphenhydramine, cardiac glycosides, and diuretics.

Grastek is contraindicated in the following conditions: severe, unstable or uncontrolled asthma, history of any severe systemic allergic reaction or any severe local reaction to sublingual allergen immunotherapy, and a history of eosinophilic esophagitis.

REFERENCES

Written by: UM Development (SE)
Date Written: 04/2014
Revised: (SF) 03/2015, 03/2016 (no clinical changes), (SE) 06/2016 (created separate Med D); (SF) 03/2017
Reviewed: Medical Affairs (KP) 04/2014 (KRU) 03/2015; (JG) 03/2017
External Review: 05/2014, 06/2015, 06/2016, 06/2017

CRITERIA FOR APPROVAL

<table>
<thead>
<tr>
<th>No.</th>
<th>Condition</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Is the requested drug being prescribed as immunotherapy for grass pollen-induced allergic rhinitis confirmed by positive skin test or <em>in vitro</em> testing for pollen-specific IgE antibodies for Timothy grass or cross-reactive grass pollens?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>Does the patient have any of the following: A) Severe, unstable, or uncontrolled asthma, B) History of any severe systemic allergic reaction or any severe local reaction to sublingual allergen immunotherapy, C) A history of eosinophilic esophagitis, D) Medical conditions that may reduce the ability of the patient to survive a serious allergic reaction or increase the risk of adverse reactions after epinephrine administration, E) Patient is on any medication(s) that can inhibit or potentiate the effect of epinephrine?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>Is the requested drug being prescribed by or in consultation with an allergist/immunologist?</td>
<td>Yes</td>
<td>No</td>
</tr>
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</table>
## Guidelines for Approval

### Duration of Approval
6 Months

#### 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>
<tr>
<td>3</td>
<td></td>
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</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>
</table>
| 1. Go to 2 | Deny | Your plan covers this drug when it is being used for the following: - immunotherapy for grass pollen-induced allergic rhinitis confirmed by positive skin test or in vitro testing for pollen-specific IgE antibodies for Timothy grass or cross-reactive grass pollens  

Your use of this drug does not meet the requirements. This is based on the information we have. |
| 2. Deny | Go to 3 | Your plan covers this drug when you do not have one of these conditions:  

--- Severe, unstable, or uncontrolled asthma  
--- History of any severe systemic allergic reaction or any severe local reaction to sublingual allergen immunotherapy  
--- A history of eosinophilic esophagitis  
--- Medical conditions that may reduce the ability of the patient to survive a serious allergic reaction or increase the risk of adverse reactions after epinephrine administration  
--- Patient is on any medication(s) that can inhibit or potentiate the effect of epinephrine  

Your use of this drug does not meet the requirements. This is based on the information we have. |
| 3. Approve, 6 months | Deny | Your plan covers this drug when it is prescribed by or working with an allergist/immunologist. Your use of this drug does not meet the requirements. This is based on the information we have. |
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 (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

* 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:
         i. 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:
   a. 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 following criteria are met:
1. The diagnosis of Prader-Willi syndrome was confirmed by genetic testing demonstrating any of the following:
   a. Deletion in the chromosomal 15q11.2-q13 region
   b. Maternal uniparental disomy in chromosome 15
   c. 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.
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.
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)

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:

1. Member has C1 inhibitor deficiency as confirmed by laboratory testing.
2. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
   a. Member has an F12 gene mutation as confirmed by genetic testing, or
   b. Member has a family history of angioedema and the angioedema was refractory to a trial of antihistamine (e.g., cetirizine) for at least one month.

III. 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. Human epidermal growth factor receptor (HER2)-negative recurrent or metastatic breast cancer
   b. HER2-positive recurrent or metastatic breast cancer
2. Soft tissue sarcoma
   a. Angiosarcoma
   b. Retroperitoneal/intra-abdominal
   c. Rhabdomyosarcoma
   d. Extremities, superficial trunk or head and 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. Extremities, superficial trunk or head and neck soft tissue 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

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 with or without ribavirin for the treatment of patients with chronic hepatitis C virus (HCV) genotype 1, 4, 5 or 6 infection.

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

II. EXCLUSIONS

Use with other drugs containing sofosbuvir, including Sovaldi.

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, without ribavirin

1. Genotype 1 infection
   a. Authorization of up to 12 weeks total may be granted for treatment-naïve members with compensated cirrhosis, HIV co-infection, African Americans or those with known IL28B polymorphism CT or TT.
   b. 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 a fibrosis score >F1.
   c. Authorization of up to 12 weeks total may be granted for treatment-naïve members without cirrhosis who have pre-treatment HCV RNA greater than or equal to 6 million IU/mL and a fibrosis score >F1.
   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.
   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
   a. Authorization of up to 12 weeks total may be granted for treatment-naïve members without cirrhosis or with compensated cirrhosis and a fibrosis score >F1.
   b. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor.
   c. 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.

3. Genotype 5 infection
   Authorization of up to 12 weeks total may be granted for members who are treatment-naïve with fibrosis score >F1 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 who are treatment-naïve with a fibrosis score >F1 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 or 4 infection and documented anemia (baseline Hgb below 10 g/dL) or RBV ineligibility (see Section V).

6. Recurrent HCV infection post liver transplantation
   Authorization of up to 24 weeks total may be granted for treatment-naive members who have recurrent HCV genotype 1 or 4 infection post liver transplantation and documented anemia (baseline Hgb below 10 g/dL) or RBV ineligibility (see Section V).

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 plus RBV with or without PEG-IFN.
      c. Authorization of up to 24 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with sofosbuvir plus RBV with or without PEG-IFN.
      d. Authorization of up to 24 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with sofosbuvir plus simeprevir with or without RBV and do not have any NS5A inhibitor resistance-associated variants (RAVs) associated with ledipasvir resistance.
      e. Authorization of up to 24 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with an HCV NS5A inhibitor and do not have any NS5A inhibitor RAVs associated with ledipasvir resistance.

   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 or 4 infection.
      b. Authorization of up to 24 weeks total may be granted for members with HCV genotype 1 or 4 infection who failed prior treatment with a sofosbuvir-containing 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 or 4 infection post liver transplantation and who have decompensated cirrhosis.

   4. Recurrent HCV infection post liver transplantation
      Authorization of up to 12 weeks total may be granted for members with recurrent HCV genotype 1 or 4 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.

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:
   - Intolerance to RBV
   - 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

Subcutaneous Immune Globulin (SCIG):
Hizentra®, HyQvia®, Cutaquig® and Cuvitru™

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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.

   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.3
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 received Humira or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) indicated for moderately to severely active rheumatoid arthritis in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Humira.
   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 polyarticular juvenile idiopathic arthritis (pJIA)
   1. Authorization of 24 months may be granted for members who have received Humira or any other biologic DMARD indicated for active polyarticular juvenile idiopathic arthritis in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Humira.
   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 received Humira or any other biologic DMARD indicated for active ankylosing spondylitis in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Humira.
   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) over a 4-week period in total at maximum recommended or tolerated anti-inflammatory dose.
      b. Member has an intolerance and/or contraindication to two or more NSAIDs (see Appendix B).

E. Moderately to severely active Crohn’s disease (CD)
   1. Authorization of 24 months may be granted for members who have received Humira or any other biologic indicated for the treatment of Crohn’s disease in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Humira.
   2. Authorization of 24 months may be granted for treatment of moderately to severely active CD if the following criteria is met:
      a. Member has an inadequate response, intolerance or contraindication to at least one conventional therapy option (see Appendix C).

F. Moderately to severely active ulcerative colitis (UC)
   1. Authorization of 24 months may be granted for members who have received Humira or any other biologic indicated for moderately to severely active ulcerative colitis in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Humira.
   2. Authorization of 24 months may be granted for treatment of moderately to severely active UC if the member has had an inadequate response, intolerance or contraindication to at least one conventional therapy option (see Appendix D).

G. Moderate to severe chronic plaque psoriasis (PsO)
   1. Authorization of 24 months may be granted for members who have received Humira, Otezla, or any other biologic DMARD indicated for the treatment of moderate to severe chronic plaque psoriasis in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Humira.
   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 E).
         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) in a paid claim through a pharmacy or medical benefit within the previous 120 days of the continuation request 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 (male or female)
   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
Appendix C: Examples of Conventional Therapy Options for CD
1. Mild to moderate disease – induction of remission:
   a. Oral budesonide, oral mesalamine
   b. Alternatives: metronidazole, ciprofloxacin, rifaximin
2. Mild to moderate disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternatives: oral budesonide, methotrexate intramuscularly (IM)
3. Moderate to severe disease – induction of remission:
   a. Prednisone, methylprednisolone intravenously (IV)
   b. Alternatives: methotrexate IM
4. Moderate to severe disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: methotrexate IM
5. Perianal and fistulizing disease – induction of remission
   a. Metronidazole ± ciprofloxacin
6. Perianal and fistulizing disease – maintenance of remission
   a. Azathioprine, mercaptopurine
   b. Alternative: methotrexate IM

Appendix D: 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 E: 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

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 Use

SCLC

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

II. CRITERIA FOR INITIAL APPROVAL

Small cell lung cancer (SCLC)

Authorization of 12 months may be granted for treatment of SCLC.

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

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
   2. fulvestrant in women with disease progression following endocrine therapy.

B. Compendial Uses
   Soft tissue sarcoma: well-differentiated/dedifferentiated retroperitoneal 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 (eg, anastrozole, exemestane, letrozole) for a postmenopausal member
   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 retroperitoneal liposarcoma.

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 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

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 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

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. Treatment of newly diagnosed adult and pediatric patients with Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase
   2. Treatment of patients with Ph+ CML in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy
   3. Treatment of adult patients with relapsed or refractory Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL)
   4. Treatment of pediatric patients with newly diagnosed Ph+ ALL in combination with chemotherapy
   5. Treatment of 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. Treatment of 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. Treatment of 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. Treatment of adult patients with unresectable, recurrent and/or metastatic dermatofibrosarcoma protuberans (DFSP)
   9. Treatment of 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. 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. Ph+ ALL/lymphoblastic lymphoma
   4. DFSP, for adjuvant treatment following resection
   5. GIST (primary, preoperative, postoperative and continued treatment)
   6. Desmoid tumors
   7. Pigmented villonodular synovitis/tenosynovial giant cell tumor
   8. Chordoma
   9. C-Kit mutated melanoma

All other indications are considered experimental/investigational and are not a covered benefit.
II. CRITERIA FOR INITIAL APPROVAL

A. Chronic Myelogenous Leukemia (CML)
Authorization of 12 months may be granted for members initiating Gleevec for the treatment of CML when BOTH of the following criteria are met:
1. Diagnosis of CML was confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing
2. 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
Authorization of 12 months may be granted for members initiating Gleevec for the treatment of Ph+ ALL/lymphoblastic lymphoma when diagnosis of Ph+ ALL/lymphoblastic lymphoma was 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 members initiating Gleevec for the treatment of GIST, desmoid tumors, PVNS/TGCT, HES/CEL, DFSP, or chordoma

D. Myelodysplastic Syndromes and Myeloproliferative Diseases (MDS/MPD)
Authorization of 12 months may be granted for members initiating Gleevec for the treatment of MDS or MPD when the member’s disease is associated with PDGFR gene rearrangements

E. Aggressive Systemic Mastocytosis (ASM)
Authorization of 12 months may be granted for members initiating Gleevec for the 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 members initiating Gleevec for the treatment of c-Kit mutation-positive melanoma

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet ALL diagnosis-specific authorization criteria below:

A. Chronic Myelogenous Leukemia (CML)
Authorization of up to 12 months may be granted for members continuing Gleevec for the treatment of CML when ALL of the following criteria are met:
1. Diagnosis of CML was confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing
2. Member did not fail (other than due to intolerance) prior therapy with a TKI (e.g., dasatinib, nilotinib, bosutinib, ponatinib)
3. Member meets ANY of the following criteria:
   a. Authorization of up to 12 months for members with chronic phase CML if receiving benefit from Gleevec therapy (i.e., achieved or maintained a cytogenic or molecular response to therapy).
   b. Authorization of 12 months for members with accelerated or blast phase CML
   c. Authorization of 12 months for members who have received a HSCT for CML (any phase)
B. Ph+ Acute Lymphoblastic Leukemia (ALL)/lymphoblastic lymphoma, Melanoma, Myelodysplastic Syndromes and Myeloproliferative Diseases (MDS/MPD), Aggressive Systemic Mastocytosis (ASM), 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

All members (including new members) requesting authorization for continuation of Gleevec therapy for Ph+ ALL, melanoma, MDS/MPD, ASM, GIST, desmoid tumors, PVNS/TGCT, HES/CEL, DFSP or chordoma must meet ALL initial authorization criteria

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

FDA-APPROVED INDICATIONS
Belsomra (suvorexant) is indicated for the treatment of insomnia characterized by difficulties with sleep onset and/or sleep maintenance.

COVERAGE CRITERIA
Belsomra (suvorexant) will be covered with prior authorization when the following criteria are met:
- The drug is being prescribed for the treatment of insomnia characterized by difficulties with sleep onset and/or sleep maintenance
- 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)
- The patient does not have a diagnosis of narcolepsy
- If the patient is 65 years of age or older, the patient experienced an inadequate treatment response, intolerance or contraindication to Rozerem, Silenor or trazodone
- 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., zolpidem) and a short acting benzodiazepine (e.g., temazepam)

Quantity Limits may apply.

RATIONALE
Belsomra (suvorexant) is indicated for the treatment of insomnia characterized by difficulties with sleep onset and/or sleep maintenance.

Use the lowest dose effective for the patient. 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. The Food and Drug Administration (FDA) recommends that physicians advise patients against next-day driving because of the potential for somnolence if they are taking double the recommended dose. It is also recommended that patients on lower doses still should be cautioned about the potential for driving impairment, but did not recommend against driving.

Belsomra (suvorexant) is contraindicated in patients with narcolepsy. Belsomra (suvorexant) will be supplied in unit-of-use blisters of 30 with the possibility of the package not being split; therefore, Belsomra (suvorexant) will not be included in the Insomnia Limit criteria.

Insomnia is defined as complaints of disturbed sleep in the presence of adequate opportunity and circumstance for sleep. The disturbance can consist of difficulty in falling asleep; frequent awakenings, difficulty returning to sleep, awakening too early in the morning, or sleep that does not feel restful, refreshing, or restorative. Insomnia can be primary or secondary to a variety of medical illnesses, psychiatric disorders, or drug use. Identifying and treating potential underlying conditions...
or comorbid diagnoses are priorities in the treatment of insomnia. In order to treat insomnia, various treatment modalities should be considered, such as, sleep hygiene, sleep restriction, stimulus control, and cognitive behavioral therapy, prior to the addition of pharmacotherapy, and continued throughout pharmacotherapy treatment. The American College of Physicians (ACP) recommends that all adult patients receive cognitive behavioral therapy for insomnia (CBT-I) as the initial treatment for chronic insomnia disorder. The goal of treatment for insomnia is to improve sleep and alleviate distress or dysfunction caused by the disorder.

The treatment of insomnia should be individualized and is dependent on the differential diagnosis. Although short-term therapy is appropriate for most patients, some patients may benefit from long-term use. Patients with insomnia lasting more than a month may have the diagnosis of chronic 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 3 nights per week for at least 3 months; and not be linked to other sleep, medical, or mental disorders. There are indications that long-term management of chronic insomnia may be beneficial. Long-term management of chronic insomnia is achievable when pharmacotherapy is considered for use only in response to the occurrence of the symptoms, thus permitting long-term therapy without the use of nightly medication.

Guidelines for prescribing hypnotics
- Initiate hypnotic use with identifying and addressing specific behaviors, circumstances, and underlying disorders contributing to insomnia
- Use the lowest effective dose
- Prescribe hypnotics for short durations (two to four weeks) and intermittently (based on patient’s return to an acceptable sleep cycle)
- Watch for requests for escalating doses or resistance to tapering or discontinuing hypnotic
- Discontinue hypnotics gradually

In addition, the patient should be evaluated frequently and monitored for efficacy, side effects, tolerance and abuse/misuse of the medication. Clinicians should revisit the need for medication continuation at periodic intervals.

Periodic attempts to reduce the frequency and dose in order to minimize side effects and determined the lowest effective dose may be indicated.

The American Academy of Sleep Medicine (AASM) guidelines for the evaluation and management of chronic insomnia in adults recommend the following general sequence of medication trials (Consensus): short-intermediate acting benzodiazepines (BZDs), non-BZDs or ramelteon, followed by sedating antidepressants, combined BZD or ramelteon and sedating antidepressant.

Therefore, 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., zolpidem) and a short acting benzodiazepine (e.g., temazepam) 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. Examples included are short acting benzodiazepines and non-benzodiazepine sedative hypnotics. Therefore, coverage will be provided for Belsomra.
(suvorexant) in patients 65 years of age or older for the treatment of insomnia when an inadequate treatment response, intolerance or contraindication to Rozerem, Silenor or trazodone has been demonstrated.

**REFERENCES**


**CRITERIA FOR APPROVAL**

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Is the drug being prescribed for the treatment of insomnia characterized by difficulties with sleep onset and/or sleep maintenance?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>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)?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>3. Does the patient have a diagnosis of narcolepsy?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>4. Is the patient 65 years of age or older?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>[If no, then skip to question 6.]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Has the patient experienced an inadequate treatment response, intolerance or contraindication to Rozerem, Silenor or trazodone?</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>
Has the patient experienced an inadequate treatment response, intolerance or contraindication to a generic non-benzodiazepine sedative-hypnotic (e.g., zolpidem) and a short acting benzodiazepine (e.g., temazepam)?

Yes  No

Does the patient require use of MORE than 30 tablets per month of Belsomra (suvorexant)?

Yes  No

[Tech Note: If yes, then deny and enter a partial approval for 30 tablets per 25 days or 90 tablets per 75 days]

<table>
<thead>
<tr>
<th>Mapping Instructions</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DENIAL REASONS – DO NOT USE FOR MEDICARE PART D</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Go to 2</td>
<td>Deny</td>
<td>Your plan covers this drug when you have insomnia. Your use of this drug does not meet the requirement. This is based on the information we have.</td>
</tr>
<tr>
<td>2. Go to 3</td>
<td>Deny</td>
<td>Your plan covers this drug when other reasons for insomnia have been addressed. Your use of this drug does not meet the requirement. This is based on the information we have.</td>
</tr>
<tr>
<td>3. Deny</td>
<td>Go to 4</td>
<td>Your plan does not cover this drug when you have narcolepsy. Your use of this drug does not meet the requirement. This is based on the information we have.</td>
</tr>
<tr>
<td>4. Go to 5</td>
<td>Go to 6</td>
<td></td>
</tr>
</tbody>
</table>
| 5. Go to 7 | Deny | Your plan covers this drug when you meet all of these conditions:  
- You are 65 years of age or older  
- You tried another drug for insomnia first (Rozerem, Silenor or trazodone)  
- The other drug did not work for you or you cannot use it  
Your use of this drug does not meet the requirements. This is based on the information we have. |
| 6. Go to 7 | Deny | 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 (e.g., zolpidem) and a short acting benzodiazepine (e.g., temazepam)  
- The other drug did not work for you or you cannot use it  
Your use of this drug does not meet the requirements. This is based on the information we have. |
| 7. 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. Your request for additional quantities of the requested drug and strength has been denied. |
PRIOR AUTHORIZATION CRITERIA

DRUG CLASS  INSOMNIA AGENTS

BRAND NAME  EDLUAR SUBLINGUAL TABLETS  (zolpidem)
(generic)

INTERMEZZO SUBLINGUAL TABLETS  (zolpidem)

ZOLPIMIST ORAL SPRAY  (zolpidem)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization  Ref # 387-C

FDA-APPROVED INDICATIONS
Edluar
Edluar sublingual tablets are indicated for the short-term treatment of insomnia characterized by difficulties with sleep initiation. The clinical trial 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 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
AND
• The patient does not require MORE than 30 tablets per month of Edluar (zolpidem) sublingual tablets or 1 container of ZolpiMist (zolpidem) oral spray
OR
Intermezzo (zolpidem) sublingual tablets 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: male, 65 years of age and under, or not taking Intermezzo (zolpidem)
  sublingual tablets concomitantly with other CNS depressants (e.g., benzodiazepines, opioids, tricyclic
  antidepressants, alcohol)

AND

• The patient does not require MORE than 30 tablets per month of Intermezzo (zolpidem) sublingual tablets 1.75
  mg or 3.5 mg

OR

• The patient is one of the following: female, over 65 years old or taking Intermezzo (zolpidem) sublingual tablets
  concomitantly with other CNS depressants (e.g., benzodiazepines, opioids, tricyclic antidepressants, alcohol)

AND

  • The request is for the 1.75 mg strength for a dose not exceeding 1.75 mg per day

AND

• The patient does not require MORE than 30 tablets per month of Intermezzo (zolpidem) sublingual tablets 1.75
  mg

Quantity Limits may apply.

RATIONALE

ZolpiMist (zolpidem) and Edluar (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. ZolpiMist (zolpidem) and Edluar (zolpidem) will be
allowed for the treatment of insomnia characterized by difficulties with sleep initiation when other potential causes of sleep
disturbances have been addressed.

Intermezzo (zolpidem) sublingual tablets are 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 allowed 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.

The recommended initial dose of Edluar (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) should not exceed 10 mg once daily immediately before bedtime. The recommended initial
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 initial dose of 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 ZolpiMist (zolpidem) should not exceed 10 mg once daily immediately before bedtime. The recommended
initial 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. 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.
The Food and Drug Administration (FDA) recommends that the bedtime dose of zolpidem be lowered because new data show that blood levels in some patients may be high enough the morning after use to impair activities that require alertness, including driving.

Insomnia is defined as complaints of disturbed sleep in the presence of adequate opportunity and circumstance for sleep. The disturbance can consist of difficulty in falling asleep; frequent awakenings, difficulty returning to sleep, awakening too early in the morning, or sleep that does not feel restful, refreshing, or restorative. Insomnia can be primary or secondary to a variety of medical illnesses, psychiatric disorders, or drug use. Identifying and treating potential underlying conditions or comorbid diagnoses are priorities in the treatment of insomnia. In order to treat insomnia, various treatment modalities should be considered, such as, sleep hygiene, sleep restriction, stimulus control, and cognitive behavioral therapy, prior to the addition of pharmacotherapy, and continued throughout pharmacotherapy treatment. The American College of Physicians (ACP) recommends that all adult patients receive cognitive behavioral therapy for insomnia (CBT-I) as the initial treatment for chronic insomnia disorder. The goal of treatment for insomnia is to improve sleep and alleviate distress or dysfunction caused by the disorder.

The treatment of insomnia should be individualized and is dependent on the differential diagnosis. Although short-term therapy is appropriate for most patients, some patients may benefit from long-term use. Patients with insomnia lasting more than a month may have the diagnosis of chronic 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 3 nights per week for at least 3 months; and not be linked to other sleep, medical, or mental disorders. There are indications that long-term management of chronic insomnia may be beneficial. Long-term management of chronic insomnia is achievable when pharmacotherapy is considered for use only in response to the occurrence of the symptoms, thus permitting long-term therapy without the use of nightly medication.

Guidelines for prescribing hypnotics. 
- Initiate hypnotic use with identifying and address specific behaviors, circumstances, and underlying disorders contributing to insomnia
- Use the lowest effective dose
- Prescribe hypnotics for short durations (two to four weeks) and intermittently (based on patient's return to an acceptable sleep cycle)
- Watch for requests for escalating doses or resistance to tapering or discontinuing hypnotic
- Discontinue hypnotics gradually

In addition, the patient should be evaluated frequently and monitored for efficacy, side effects, tolerance and abuse/misuse of the medication. Clinicians should revisit the need for medication continuation at periodic intervals. Periodic attempts to reduce the frequency and dose in order to minimize side effects and determined the lowest effective dose may be indicated.

REFERENCES


### CRITERIA FOR APPROVAL

**ZOLPIMIST AND EDLUAR:**

1. Is the drug being prescribed for insomnia characterized by difficulties with sleep initiation?  
   - **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 unable to swallow tablets/capsules?  
   - **Yes**
   - **No**

4. 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**

   [Tech 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.]

### Mapping Instructions

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
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</thead>
<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>Deny</td>
</tr>
<tr>
<td>2. Go to 3</td>
<td>Deny</td>
</tr>
<tr>
<td>3. Go to 4</td>
<td>Deny</td>
</tr>
</tbody>
</table>
| 4. Deny | Approve, 36 months Edluar - 30 sublingual tabs/25 days or 90 sublingual tabs/75 days 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/month of Edluar (zolpidem sublingual tablets) or  
- 1 container/month of ZolpiMist (zolpidem oral spray)  
You have been approved for the maximum quantity that your plan covers. Your request for additional quantities of the requested drug and strength has been denied. |
CRITERIA FOR APPROVAL

INTERMEZZO:

1. Is the drug being prescribed for insomnia when middle-of-the-night awakening is followed by difficulty returning to sleep?  
   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 one of the following: A) female, B) over 65 years old, C) taking the requested drug concomitantly with other CNS depressants (e.g., benzodiazepines, opioids, tricyclic antidepressants, alcohol)?  
   [If yes, then go to question 5.]
   Yes    No

4. Does the patient require use of MORE than 30 tablets per month of Intermezzo (zolpidem) sublingual tablets 1.75 mg or 3.5 mg?  
   [No further questions.]
   [Tech 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.]
   Yes    No

5. Is the request for the 1.75 mg strength for a dose not exceeding 1.75 mg per day?  
   Yes    No

6. Does the patient require use of MORE than 30 tablets per month of Intermezzo (zolpidem) sublingual tablets 1.75 mg?  
   [Tech 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.]
   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. Go to 2</td>
<td>Deny</td>
<td>Your plan covers this drug when you have insomnia. Your use of this drug does not meet the requirement. This is based on the information we have.</td>
</tr>
<tr>
<td>2. Go to 3</td>
<td>Deny</td>
<td>Your plan covers this drug when other reasons for insomnia have been addressed. Your use of this drug does not meet the requirement. This is based on the information we have.</td>
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<tr>
<td>3. Go to 5</td>
<td>Go to 4</td>
<td></td>
</tr>
<tr>
<td>4. Deny</td>
<td>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</td>
<td>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. Your request for additional quantities of the requested drug and strength has been denied.</td>
</tr>
</tbody>
</table>
| 5. Go to 6 | Deny | Your plan covers this drug if you meet one of the following:  
- You are male  
- You are 65 years old and under  
- You are not taking this drug at the same time as another CNS depressants (e.g., benzodiazepines, opioids, tricyclic antidepressants, alcohol) OR  
- You are 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  
- You are not taking more than 1.75 mg per day. Your use of this drug does not meet the requirements. This is based on the information we have. |
| 6. Deny | 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. Your request for additional quantities of the requested drug and strength has been denied. |
PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>ISOTRETINOINS (ALL ORAL)</th>
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</thead>
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<tr>
<td>BRAND NAME</td>
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<td>AMNESTEEM (isotretinoin)</td>
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<td>CLARAVIS (isotretinoin)</td>
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<td>MYORISAN (isotretinoin)</td>
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<td>SOTRET (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

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 Disease) – severe

COVERAGE CRITERIA
Isotretinoin will be covered with prior authorization when the following criteria are met:

- The patient has the diagnosis of acne vulgaris (severe recalcitrant nodular or refractory) OR severe refractory rosacea AND
  - The patient has tried and had 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 neuroblastoma, OR cutaneous T-cell lymphoma (CTCL) (e.g., mycosis fungoides, Sezary syndrome), OR is at high risk for developing skin cancer (squamous cell cancers)

OR
- The requested drug is being prescribed for any of the following: A) transient acantholytic dermatosis (Grover Disease), B) keratosis follicularis (Darier Disease), C) lamellar ichthyosis, D) pityriasis rubra pilaris

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. 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.

Isotretinoin must not be used by female patients who are or may become pregnant. Because of isotretinoin teratogenicity and to minimize fetal exposure, isotretinoin is approved for marketing only under a special restricted distribution program approved by the Food and Drug Administration. This program is called iPLEDGE. Isotretinoin must only be prescribed by prescribers who are registered and activated with the iPLEDGE program. Isotretinoin must only be dispensed by a pharmacy registered and activated with iPLEDGE, and must only be dispensed to patients who are registered and meet all the requirements of iPLEDGE.

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.1-10 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.7,8

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.7, 8, 13

The National Comprehensive Cancer Network 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. 7,8,14,16

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). 7,8,15,16

Isotretinoin has been used in the treatment of transient acantholytic dermatosis (Grover’s Disease), keratosis follicularis (Darier Disease), lamellar ichthyosis, pityriasis rubra pilaris, and rosacea 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. 7, 8

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.7,8,11,12

For transient acantholytic dermatosis 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 (acitretin or isotretinoin) has been reported. More troubling eruptions usually clear up after taking isotretinoin or tetracycline for one to three months.7,8,17-19

For 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 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. 7,8,20,21

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. 7,8,22

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. 7,8,23,24
REFERENCES

**CRITERIA FOR APPROVAL**

1. Does the patient have the diagnosis of acne vulgaris (severe recalcitrant nodular or refractory) OR severe refractory rosacea?  
   [If no, then skip to question 4.]
   - Yes
   - No

2. Has the patient tried and had 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 neuroblastoma, OR cutaneous T-cell lymphoma (CTCL) (e.g., mycosis fungoides, Sezary syndrome), OR is at high risk for developing skin cancer (squamous cell cancers)?  
   [If yes, then no further questions.]
   - Yes
   - No

5. Is the requested drug being prescribed for any of the following: A) transient acantholytic dermatosis (Grover Disease), B) keratosis follicularis (Darier Disease), C) lamellar ichthyosis, D) pityriasis rubra pilaris?  
   - Yes
   - No

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### Guidelines for Approval

<table>
<thead>
<tr>
<th>Duration of Approval</th>
<th>12 Months</th>
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<tbody>
<tr>
<td><strong>Set 1</strong></td>
<td><strong>Set 2</strong></td>
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<tr>
<td>Yes to question(s)</td>
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### Mapping Instructions

<table>
<thead>
<tr>
<th>Denial Reasons – Do Not Use for Medicare Part D</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Yes</strong></td>
</tr>
<tr>
<td>1. Go to 2</td>
</tr>
</tbody>
</table>
| 2. Go to 3 | **Deny** | Your plan covers this drug when you meet all of these conditions:
- You have acne or severe refractory rosacea
- You tried another topical acne product first, which did not work for you
- You tried an oral antibiotic first, which did not work for you
Your use of this drug does not meet these requirements. This is based on the information we have. |
| 3. Approve, 12 Months | **Deny** | Your plan covers this drug when you do not use the drug for more than 40 weeks total with an 8-week break. Your use of this drug does not meet the requirement. This is based on the information we have. |
| 4. Approve, 12 Months | Go to 5 |
| 5. Approve, 12 Months | **Deny** | Your plan covers this drug when you meet one of these conditions:
- You have acne
- You have severe refractory rosacea
- You have neuroblastoma |
- You have cutaneous T-cell lymphoma
- You are at high risk for developing skin cancer
- You have transient acantholytic dermatosis (Grover Disease)
- You have keratosis follicularis (Darier Disease)
- You have lamellar ichthyosis
- You have pityriasis rubra pilaris

Your use of this drug does not meet these requirements. This is based on the information we have.
PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>ITRACONAZOLE TABLETS</th>
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<tbody>
<tr>
<td>BRAND NAME</td>
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<td>(itraconazole tablets)</td>
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**Status:** CVS Caremark Criteria

**Type:** Initial Prior Authorization

**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**
Onmel will be covered with prior authorization when the following criteria are met:
- The patient does not have any of the following: A) Evidence of ventricular dysfunction, such as congestive heart failure (CHF), B) Current use of certain drugs metabolized by cytochrome P450 3A4 (CYP3A4) AND
- Onmel is being requested 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.

Onmel is contraindicated in patients with evidence of ventricular dysfunction such as congestive heart failure (CHF) or a history of CHF. Coadministration of Onmel (itraconazole) and cisapride, doxepilide, ergot alkaloids such as dihydroergotamine, ergotamine, ergometrine (ergonovine), and methylergometrine (methylergonovine), felodipine, levacetylmethadol, lovastatin, methadone, oral midazolam, nisoldipine, pimozide, quinidine, simvastatin, or triazolam are contraindicated.

**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)
Reviewed: Medical Affairs: (DNC) 01/2013; (DNC) 08/2013; (LCB) 09/2014; (LS) 05/2015
External Review: 01/2013, 02/2013, 12/2013, 10/2014, 10/2015, 08/2016

Itraconazole (Onmel Tablets) MDC.doc
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## CRITERIA FOR APPROVAL

1. Does the patient have any of the following: A) Evidence of ventricular dysfunction, such as congestive heart failure (CHF), B) Current use of certain drugs metabolized by cytochrome P450 3A4 (CYP3A4)?
   - Yes
   - No

2. Is Onmel being requested for the treatment of onychomycosis of the toenail due to *Trichophyton* that has been confirmed by a fungal diagnostic test?
   - Yes
   - No

### Guidelines for Approval

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<th>Duration of Approval</th>
<th>3 Months</th>
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### Mapping Instructions

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<td>1. Deny</td>
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**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**

1. **Deny**
   - Your plan covers this drug when you do not have any of these conditions:
     - Heart ventricle dysfunction, such as congestive heart failure (CHF)
     - You are currently taking certain medicines
   - Your use of this drug does not meet the requirements. This is based on the information we have.

2. **Deny**
   - Your plan covers this drug when you meet all of these conditions:
     - You have a fungal infection of the toenail
     - You had a test to confirm your toenail fungus
   - Your use of this drug does not meet the requirements. This is based on the information we have.
PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>ITRACONAZOLE CAPSULES</th>
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<tr>
<td>BRAND NAME</td>
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<td>(itraconazole)</td>
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Status: CVS Caremark Criteria
Type: Initial Prior Authorization
MDC-1
Ref # 280-A

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 manuum/Tinea pedis

COVERAGE CRITERIA
Sporanox capsules will be covered with prior authorization when the following criteria are met:
- Patient has the diagnosis of onychomycosis due to tinea that has been confirmed by a fungal diagnostic test.
  AND
  - The patient does not have any of the following: A) Evidence of ventricular dysfunction, such as congestive heart failure (CHF), B) Current use of certain drugs metabolized by cytochrome P450 3A4 (CYP3A4)
  OR
- The patient is not currently taking certain drugs metabolized by cytochrome P450 3A4 (CYP3A4)
  AND
- Patient has Pityriasis versicolor or Tinea versicolor.
  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 manuum, D) Tinea pedis.
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 or tinea versicolor, tinea corporis, tinea cruris, 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 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.

Sporanox (itraconazole) capsules should not be administered for the treatment of onychomycosis in patients with evidence of ventricular dysfunction such as congestive heart failure (CHF) or a history of CHF. Coadministration with certain drugs metabolized by cytochrome P450 3A4 (CYP3A4) is contraindicated.

REFERENCES


CRITERIA FOR APPROVAL

1. Does the patient have the diagnosis of onychomycosis due to tinea that has been confirmed by a fungal diagnostic test? Yes  No
2. Does the patient have any of the following: A) Evidence of ventricular dysfunction, such as congestive heart failure (CHF), B) Current use of certain drugs metabolized by cytochrome P450 3A4 (CYP3A4)? Yes  No
3. Is the patient currently taking certain drugs metabolized by cytochrome P450 3A4 (CYP3A4)? Yes  No
4. Does the patient have Pityriasis versicolor or Tinea versicolor? Yes  No
5. Does the patient have one of the following diagnoses: A) Tinea corporis, B) Tinea cruris, C) Tinea manuum, D) Tinea pedis? Yes  No
6. Has the patient experienced an inadequate treatment response, adverse event, intolerance, or contraindication to griseofulvin? Yes  No
7. 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

Guidelines for Approval

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#### Mapping Instructions

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<th>DENIAL REASONS – DO NOT USE FOR MEDICARE PART D</th>
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</table>
| 1. Go to 2 | Go to 3 | Your plan covers this drug when you meet all of these conditions:  
- You have an infection  
- The infection is caused by a fungus  
- Tests show the fungus caused infection  
- You do not have evidence of ventricular dysfunction, such as congestive heart failure (CHF)  
- You are not currently taking certain medicines  
Your use of this drug does not meet these requirements. This is based on the information we have. |
| 2. Deny | Approve, 3 months | Your plan covers this drug when you meet all of these conditions:  
- You have an infection  
- The infection is caused by a fungus  
- Tests show the fungus caused infection  
- You do not have evidence of ventricular dysfunction, such as congestive heart failure (CHF)  
- You are not currently taking certain medicines  
Your use of this drug does not meet these requirements. This is based on the information we have. |
| 3. Deny | Go to 4 | Your plan covers this drug when you are not currently taking certain medicines.  
Your use of this drug does not meet this requirement. This is based on the information we have. |
| 4. Approve, 3 months | Go to 5 | |
| 5. Go to 6 | Go to 7 | |
| 6. Approve, 3 months | Deny | Your plan covers this drug when you have these conditions:  
- You have a yeast infection of the skin or a fungal infection of the skin  
- You have ringworm, a fungal infection of the groin, a fungal infection of the hand, or athlete’s foot AND you have had poor response to griseofulvin or cannot take it.  
Your use of this drug does not meet these requirements. This is based on the information we have. |
| 7. Approve, 6 months | Deny | Your plan covers this drug when you have these conditions:  
- You have Blastomycosis, Histoplasmosis, Aspergillosis, Coccidioidomycosis, Cryptococcosis, Sporotrichosis, Penicilliosis or Microsporidiosis  
Your use of this drug does not meet these requirements. This is based on the information we have. |
PRIOR AUTHORIZATION CRITERIA

<table>
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<tr>
<th>DRUG CLASS</th>
<th>ITRACONAZOLE SOLUTION</th>
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<tr>
<td>BRAND NAME</td>
<td>SPORANOX ORAL SOLUTION</td>
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<td>(generic)</td>
<td>(itraconazole)</td>
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Status: CVS Caremark Criteria  
Type: Initial Prior Authorization  
Ref # 210-A  

FDA-APPROVED INDICATIONS
Sporanox (itraconazole) Oral Solution is indicated for the treatment of oropharyngeal and esophageal candidiasis.

COVERAGE CRITERIA
Sporanox (itraconazole) Oral Solution will be covered with prior authorization when the following criteria are met:

- Patient has a diagnosis of oropharyngeal candidiasis or esophageal candidiasis.
- Patient is not currently using certain drugs metabolized by cytochrome P450 3A4 (CYP3A4)
- Patient has a life-threatening or serious infection
- Patient does not have a life-threatening or serious infection

AND

- Patient does not have evidence of ventricular dysfunction, such as congestive heart failure (CHF)

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. 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 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 Oral Solution and Sporanox Capsules should not be used interchangeably. Only Sporanox Oral Solution has been demonstrated effective for oral and/or esophageal candidiasis.

Sporanox (itraconazole) oral solution is contraindicated in patients with evidence of ventricular dysfunction such as congestive heart failure (CHF) or a history of CHF except for the treatment of life-threatening or other serious infections. Coadministration of Sporanox (itraconazole) oral solution and cisapride, dofetilide, ergot alkaloids such as dihydroergotamine, ergotamine, ergometrine (ergonovine), and methylergometrine (methyl ergonovine), felodipine, levacetylmethadol, lovastatin, methadone, oral midazolam, nisoldipine, pimozide, quinidine, simvastatin, or triazolam are contraindicated.
## REFERENCES


Written by: UM Development (CT)
Date Written: 12/2005

### CRITERIA FOR APPROVAL

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<th>Question</th>
<th>Yes</th>
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<tr>
<td>1. Does the patient have a diagnosis of oropharyngeal candidiasis or esophageal candidiasis?</td>
<td>Yes</td>
<td>No</td>
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<tr>
<td>2. Is the patient currently taking certain drugs metabolized by cytochrome P450 3A4 (CYP3A4)?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>[If yes, no further questions.]</td>
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<tr>
<td>3. Does the patient have a life-threatening or serious infection?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>[If yes, no further questions.]</td>
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<tr>
<td>4. Does the patient have evidence of ventricular dysfunction, such as congestive heart failure (CHF)?</td>
<td>Yes</td>
<td>No</td>
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### Guidelines for Approval

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<th>Duration of Approval</th>
<th>Set 2</th>
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### Mapping Instructions

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<tbody>
<tr>
<td>1. Go to 2</td>
<td>Deny</td>
<td>Your plan covers this drug when you have a fungal infection of the mouth or throat (Oropharyngeal candidiasis or Esophageal candidiasis). Your use of this drug does not meet these requirements. This is based on the information we have.</td>
</tr>
<tr>
<td>2. Deny</td>
<td>Go to 3</td>
<td>Your plan covers this drug when you are not taking certain drugs with it. Your use of this drug does not meet these requirements. This is based on the information we have.</td>
</tr>
<tr>
<td>3. Approve, 6 months</td>
<td>Go to 4</td>
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<tr>
<td>4. Deny</td>
<td>Approve, 6 months</td>
<td>Your plan covers this drug when you meet one of these conditions: - You have a life-threatening or serious infection - You do not have a life-threatening or serious infection or heart ventricle dysfunction, such as congestive heart failure (CHF) Your use of this drug does not meet these requirements. This is based on the information we have.</td>
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PRIOR AUTHORIZATION CRITERIA

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<th>DRUG CLASS</th>
<th>ITRACONAZOLE SOLUTION</th>
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<tr>
<td>BRAND NAME</td>
<td>SPORANOX ORAL SOLUTION</td>
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<td>(itraconazole)</td>
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Status: CVS Caremark Criteria  
Type: Initial Prior Authorization  
Ref # 1286-A

FDA-APPROVED INDICATIONS
Sporanox (itraconazole) Oral Solution is indicated for the treatment of oropharyngeal and esophageal candidiasis.

COMPENDIAL USES
- Blastomycosis^2
- Histoplasmosis^2
- Aspergillosis^2
- Coccidioidomycosis^2
- Cryptococcosis^2
- Microsporidiosis^2
- Penicilliosis^2
- Pityriasis versicolor/Tinea versicolor^2
- Sporotrichosis^2
- Tinea corporis/Tinea cruris, Tinea manuum/Tinea pedis^2

COVERAGE CRITERIA
Sporanox (itraconazole) Oral Solution will be covered with prior authorization when the following criteria are met:
- Patient is not currently taking certain drugs metabolized by cytochrome P450 3A4 (CYP3A4)  
  AND
- Patient has a life-threatening or serious infection  
  OR
- Patient does not have a life-threatening or serious infection  
  AND
  - Patient does not have evidence of ventricular dysfunction, such as congestive heart failure (CHF)  
  AND
- 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 the diagnosis of onychomycosis due to tinea that has been confirmed by a fungal diagnostic test.  
  OR
- Patient has Pityriasis versicolor or Tinea versicolor.  
  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 manuum, D) Tinea pedis.  
  AND
  - 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.

It has been recommended that Sporanox (itraconazole) Oral Solution 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 cavity 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 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 fingertip 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 or tinea versicolor, tinea corporis, tinea cruris, 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 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.

Sporanox (itraconazole) oral solution is contraindicated in patients with evidence of ventricular dysfunction such as congestive heart failure (CHF) or a history of CHF except for the treatment of life-threatening or other serious infections. Coadministration of Sporanox (itraconazole) oral solution and cisapride, doxazosin, ergot alkaloids such as dihydroergotamine, ergotamine, ergometrine (ergonovine), and methylergometrine (methylergonovine), felodipine, levacetymethadol, lovastatin, methadone, oral midazolam, nisoldipine, pimozide, quinidine, simvastatin, or triazolam are contraindicat.
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PRIOR AUTHORIZATION CRITERIA

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<th>BRAND NAME</th>
<th>JUBLIA (generic) (efinaconazole topical solution)</th>
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<td>Status:</td>
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<td>Type:</td>
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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
Jublia will be covered with prior authorization when the following criteria are met:

- Jublia is being prescribed for onychomycosis of the toenail(s) due to Trichophyton rubrum or Trichophyton mentagrophytes
- The diagnosis has been confirmed with a fungal diagnostic test (e.g., potassium hydroxide [KOH] preparation, fungal culture, or nail biopsy)
- 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.5

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.5 Oral treatment of onychomycosis is the standard of care, however, drug interactions and risk of acute liver injury can limit their use.4 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.4 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 drug being prescribed for onychomycosis of the toenail(s) due to Trichophyton rubrum or Trichophyton mentagrophytes? 
   - Yes
   - No

2. Has the diagnosis been confirmed with a fungal diagnostic test (e.g., potassium hydroxide [KOH] preparation, fungal culture, or nail biopsy)?
   - Yes
   - No

3. 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

Duration of Approval

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Mapping Instructions

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<th>DENIAL REASONS – DO NOT USE FOR MEDICARE PART D</th>
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<td>Your plan covers this drug when you have a fungal infection of the toenail(s). Your use of this drug does not meet the requirement. This is based on the information we have.</td>
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<td>2. Go to 3</td>
<td>Deny</td>
<td>Your plan covers this drug when you meet all of these conditions: - You have a fungal infection of the toenail(s) - You had a test to confirm your toenail fungus Your use of this drug does not meet the requirements. This is based on the information we have.</td>
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<td>Your plan covers this drug when you meet all of these conditions: - You have a fungal infection of the toenail(s) - You had a test to confirm your toenail fungus - You tried at least one oral medicine first and it did not work for you or you cannot use it Your use of this drug does not meet the requirements. This is based on the information we have.</td>
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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. CRITERIA FOR INITIAL APPROVAL

Indefinite authorization may be granted for treatment of acute hereditary angioedema attacks in members 12 years of age or older 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


PRIOR AUTHORIZATION CRITERIA

BRAND NAME | KERYDIN (generic) (tavaborole) topical solution
Status: CVS Caremark Criteria | MDC-1
Type: Initial Prior Authorization | Ref # 1169-A

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
Kerydin will be covered with prior authorization when the following criteria are met:
• Kerydin is being prescribed for onychomycosis of the toenail(s) due to Trichophyton rubrum or Trichophyton mentagrophytes AND
• The diagnosis 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.

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
Reviewed: Medical Affairs (LMS) 07/2014; (KU) 05/2015; (ME) 05/2016

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

1. Go to 2
   
   Deny
   - Your plan covers this drug when you have a fungal infection of the toenail(s).
   - Your use of this drug does not meet the requirement. This is based on the information we have.

2. Go to 3
   
   Deny
   - Your plan covers this drug when you meet all of these conditions:
     - You have a fungal infection of the toenail(s)
     - You had a test to confirm your toenail fungus
   - Your use of this drug does not meet the requirements. This is based on the information we have.

3. Approve, 12 months
   
   Deny
   - Your plan covers this drug when you meet all of these conditions:
     - You have a fungal infection of the toenail(s)
     - You had a test to confirm your toenail fungus
     - You tried at least one oral medicine first and it did not work for you or you cannot use it
   - Your use of this drug does not meet the requirements. This is based on the information we have.
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 received any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) indicated for moderately to severely active rheumatoid arthritis in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request.

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).
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

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.

A. FDA-Approved Indication

The Kisqali Femara Co-Pack is indicated 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.

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 to postmenopausal 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

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

Kisqali is indicated 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.

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 to postmenopausal members for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer when Kisqali is used in combination with an aromatase inhibitor.

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

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 dehydralase 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 Phe level of at least 30% 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.

FDA-Approved Indication
Kymriah is indicated for the treatment of patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse.

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

II. REQUIRED DOCUMENTATION

Testing or analysis confirming CD19 protein on the surface of the B-cell

III. CRITERIA FOR INITIAL APPROVAL

Acute lymphoblastic leukemia
Authorization of 3 months may be granted to members less than 25 years of age for treatment of B-cell precursor acute lymphoblastic leukemia (ALL) when all of the following criteria are met:
A. The disease is refractory to treatment or in second or later relapse
B. The B-cells must be CD19-positive as confirmed by testing or analysis

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

BRAND NAME
LAMISIL ORAL GRANULES
(generic)
(terbinafine)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

FDA-APPROVED INDICATIONS
Lamisil (terbinafine hydrochloride) Oral Granules are indicated for the treatment of tinea capitis in patients 4 years of age and older.

COVERAGE CRITERIA
Lamisil Granules will be covered with prior authorization when the following criteria are met:
• Lamisil oral granules are being prescribed for the treatment of tinea capitis in a patient 4 years of age or older

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. Lamisil (terbinafine) Oral Granules are indicated for the treatment of tinea capitis in patients 4 years of age and older.

Lamisil (terbinafine hydrochloride) Oral Granules should be taken once a day for 6 weeks based upon body weight.

REFERENCES

Written by: UM Development (NB)
Date Written: 11/2007
Revised: (MS) 07/2008, (SE) 07/2009, (TM) 07/2010, 08/2011, (RP) 08/2012; (TM) 08/2013, 08/2014; (MS) 05/2015, 05/2016 (no clinical changes)
# CRITERIA FOR APPROVAL

1. Are Lamisil oral granules being prescribed for the treatment of tinea capitis in a patient 4 years of age or older?  

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<tr>
<th>Question (Set 1)</th>
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## Guidelines for Approval

<table>
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<th>Duration of Approval</th>
<th>2 Months</th>
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## Mapping Instructions

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<thead>
<tr>
<th>Yes/No</th>
<th>DENIAL REASONS – DO NOT USE FOR MEDICARE PART D</th>
</tr>
</thead>
</table>
| 1. Approve, 2 months | Deny  
Your plan covers this drug when you have tinea capitis and you are 4 years of age or older.  
Your use of this drug does not meet this requirement. This is based on the information we have. |
SPECIALTY GUIDELINE MANAGEMENT

Letairis (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
Letairis is indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1):
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

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:
      • mPAP ≥ 25 mmHg
      • PCWP ≤ 15 mmHg
      • 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:
      • Post cardiac surgery
      • Chronic heart disease
      • Chronic lung disease associated with prematurity
      • Congenital diaphragmatic hernia

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with PAH who are currently receiving Letairis therapy through a paid pharmacy or medical benefit.

IV. APPENDIX

WHO Classification of Pulmonary Hypertension
WHO Group 1. Pulmonary Arterial Hypertension (PAH)
1.1 Idiopathic (IPAH)
1.2 Heritable PAH
   1.2.1 Germline mutations in the bone morphogenetic protein receptor type 2 (BMPR2)
   1.2.2 Activin receptor-like kinase type 1 (ALK1), endoglin (with or without hereditary hemorrhagic telangiectasia), Smad 9, caveolin-1 (CAV1), potassium channel super family K member-3 (KCNK3)
   1.2.3 Unknown
1.3 Drug- and toxin-induced
1.4. 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. Pulmonary veno-occlusive disease (PVOD) and/or pulmonary capillary hemangiomatosis (PCH)
1*. Persistent pulmonary hypertension of the newborn (PPHN)

WHO Group 2. Pulmonary Hypertension Owing to Left Heart Disease
2.1 Systolic dysfunction
2.2 Diastolic dysfunction
2.3 Valvular disease
2.4 Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies

WHO Group 3. Pulmonary Hypertension Owing to Lung Disease and/or Hypoxia
3.1 Chronic obstructive pulmonary disease
3.2 Interstitial lung disease
3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
3.4 Sleep-disordered breathing
3.5 Alveolar hypoventilation disorders
3.6 Chronic exposure to high altitude
3.7 Developmental abnormalities

WHO Group 4. Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

WHO Group 5. Pulmonary Hypertension with Unclear Multifactorial Mechanisms
5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders, splenectomy
5.2 Systemic disorders: sarcoidosis, pulmonary Langerhans cell histiocytosis: lymphangioleiomyomatosis, neurofibromatosis, vasculitis
5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
5.4 Others: tumoral obstruction, fibrosing mediastinitis, chronic renal failure on dialysis, segmental PH

V. 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
   1. Rescue treatment after high-dose methotrexate therapy in osteosarcoma, dedifferentiated chondrosarcoma, high-grade undifferentiated pleomorphic sarcoma, peripheral T-cell lymphomas, adult T-cell leukemia/lymphoma, nasal type extranodal NK/T-cell lymphoma, mantle cell lymphoma, AIDS-related B-cell lymphomas, Burkitt lymphoma, acute lymphoblastic leukemia, primary CNS lymphoma, brain metastases, and leptomeningeal metastases
   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, and bladder cancer 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 12 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. 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)

LOTRONEX (alosetron)

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

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
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?

Yes  No

Mapping Instructions

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<tr>
<th>Yes</th>
<th>No</th>
<th>DENIAL REASONS – DO NOT USE FOR MEDICARE PART D</th>
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<tr>
<td>1.</td>
<td></td>
<td>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:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- You have had IBS symptoms for at least 6 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Gastrointestinal tract abnormalities have been ruled out</td>
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<td></td>
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<td>- Other therapies did not work for you</td>
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<tr>
<td>1.</td>
<td>Deny</td>
<td>Your use of this drug does not meet these requirements. This is based on the information we have.</td>
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Approve, 36 Months
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

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

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. 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
   6. 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)
Authorization of 6 months may be granted for treatment of ALL.

B. Acute nonlymphocytic leukemia (ANLL)
Authorization of 6 months may be granted for treatment of ANLL, including acute myeloid leukemia (AML) and acute promyelocytic leukemia (APL).

C. Multiple sclerosis
Authorization of 1 dose (3 months) may be granted for treatment of multiple sclerosis.

D. Prostate cancer
Authorization of 6 months may be granted for treatment of prostate cancer.

E. Breast cancer
Authorization of 6 months may be granted for treatment of breast cancer.

F. Hodgkin lymphoma
Authorization of 6 months may be granted for treatment of Hodgkin lymphoma.

G. Liver carcinoma
Authorization of 6 months may be granted for treatment of liver carcinoma.

H. Non-Hodgkin’s lymphoma (NHL)
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 cancer
Authorization of 6 months may be granted for treatment of ovarian 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

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

A. Non-Hodgkin’s Lymphoma (NHL)
Authorization of 6 months may be granted for the treatment of NHL when ALL of the following criteria are met:
1. Mozobil will be used to mobilize hematopoietic stem cells for collection prior to autologous transplantation
2. Mozobil will be used in combination with G-CSF (e.g., filgrastim, pegfilgrastim)

B. Multiple Myeloma
Authorization of 6 months may be granted for the treatment of multiple myeloma when ALL of the following criteria are met:
1. Mozobil will be used to mobilize hematopoietic stem cells for collection prior to autologous transplantation
2. 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

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

NEUPOGEN (filgrastim)
GRANIX (tbo-filgrastim)
ZARXIO (filgrastim-sndz)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
   a. 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
   a. 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
   a. 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
   a. 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
   a. 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.

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)
   1. Treatment of chemotherapy-induced febrile neutropenia in patients with non-myeloid malignancies
   2. Treatment of symptomatic anemia in patients with myelodysplastic syndromes (MDS), in combination with epoetin or darbepoetin
   3. Treatment of neutropenia in patients with MDS and recurrent or resistant infections
   4. Following chemotherapy for acute lymphocytic leukemia (ALL)
   5. Leukemic relapse following allogeneic stem cell transplantation
   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 currently receiving or will be receiving myelosuppressive anti-cancer therapy
   2. Neupogen/Granix/Zarxio 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

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. Advanced renal cell carcinoma (RCC)
   2. Unresectable hepatocellular carcinoma (HCC)
   3. Locally recurrent or metastatic, progressive, differentiated thyroid carcinoma (DTC) that is refractory to radioactive iodine treatment

B. Compendial Uses
   1. HCC
      a. Patients who are nontransplant candidates with unresectable disease
      b. Patients who are inoperable by performance status or comorbidity
      c. Patients who have extensive liver tumor burden or metastatic disease
   2. Acute myeloid leukemia
   3. Soft tissue sarcoma subtypes:
      a. Angiosarcoma
      b. Desmoid tumors (aggressive fibromatosis)
      c. Gastrointestinal stromal tumors (GIST)
   4. Relapsed or stage IV RCC
   5. Medullary thyroid carcinoma
   6. Osteosarcoma
   7. Chordoma

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

II. CRITERIA FOR INITIAL APPROVAL

A. Hepatocellular Carcinoma
   Authorization of 12 months may be granted for treatment of hepatocellular carcinoma.

B. Acute Myeloid Leukemia
   Authorization of 12 months may be granted for treatment of relapsed or refractory acute myeloid leukemia when the member has FLT3-ITD mutation-positive disease.

C. Soft Tissue Sarcoma (STS)
   Authorization of 12 months may be granted for treatment of soft tissue sarcoma when the STS subtype is: gastrointestinal stromal tumor (GIST), angiosarcoma, or desmoid tumor/aggressive fibromatosis
D. Renal Cell Carcinoma
Authorization of 12 months may be granted for treatment of relapsed, metastatic, or unresectable renal cell carcinoma.

E. Thyroid Carcinoma
Authorization of 12 months may be granted for treatment of medullary, papillary, Hurthle cell, or follicular thyroid carcinoma.

F. Osteosarcoma
Authorization of 12 months may be granted for treatment of osteosarcoma.

G. Chordoma
Authorization of 12 months may be granted for treatment of chordoma.

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

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

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
Basal cell carcinoma:
1. High-risk disease if residual disease is present and further surgery and radiation are contraindicated or if negative margins are unachievable by Mohs surgery or more extensive surgical procedures
2. Nodal or distant metastases

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 basal cell 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

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 12 months may be granted for treatment of idiopathic pulmonary fibrosis when all of the following criteria are met:
1. The member has undergone a diagnostic work-up which includes the following:
   a. The member does not have a known etiology for interstitial lung disease such as sarcoidosis, scleroderma, polymyositis/dermatomyositis, systemic lupus erythematosus, bronchiolitis obliterans organizing pneumonia, or drug toxicity AND
   i. The member has completed a high-resolution computed tomography (HRCT) study of the chest or surgical lung biopsy which reveals a result consistent with the usual interstitial pneumonia (UIP) pattern, OR
   ii. The member has completed an HRCT study of the chest which reveals a result consistent with the possible UIP pattern and the diagnosis is supported by surgical lung biopsy (SLB). If SLB has not been previously conducted, the diagnosis is supported by a multidisciplinary discussion between a radiologist and pulmonologist who are experienced in IPF.
2. Ofev will not be used in combination with Esbriet.

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 12 months when all of the following criteria are met:
1. The member is currently receiving treatment with Ofev through health insurance (excludes obtainment as samples or via manufacturer’s patient assistance programs).
2. Ofev will not be used in combination with Esbriet.

IV. 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

## STEP THERAPY CRITERIA

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>EXTENDED RELEASE OPIOID ANALGESICS (BRAND AND GENERIC)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRAND NAME</td>
<td>(generic)</td>
</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>
<td>(buprenorphine buccal film)</td>
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<tr>
<td>BUTTRANS</td>
<td>(buprenorphine transdermal system)</td>
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<tr>
<td>CONZIP</td>
<td>(tramadol hydrochloride extended-release)</td>
</tr>
<tr>
<td>DOLOPHINE 5 MG, 10 MG</td>
<td>(methadone hydrochloride tablets)</td>
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<tr>
<td>DURAGESIC</td>
<td>(fentanyl transdermal system)</td>
</tr>
<tr>
<td>EMBEDA</td>
<td>(morphine sulfate and naltrexone hydrochloride extended-release)</td>
</tr>
<tr>
<td>EXALGO</td>
<td>(hydromorphone hydrochloride extended-release)</td>
</tr>
<tr>
<td>HYSINGLA ER</td>
<td>(hydrocodone bitartrate extended-release tablets)</td>
</tr>
<tr>
<td>KADIAN</td>
<td>(morphine extended-release capsules)</td>
</tr>
<tr>
<td>METHADONE 5 MG/5 ML &amp; 10 MG/5 ML ORAL SOLN, 200 MG/20 ML INJ</td>
<td>(methadone hydrochloride injection; oral solution)</td>
</tr>
<tr>
<td>METHADONE INTENSOL 10 MG/ML</td>
<td>(methadone oral concentrate)</td>
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</tbody>
</table>
METHADOSE 5 MG, 10 MG  
(methadone hydrochloride tablets)

MORPHABOND  
(morphine extended-release tablets)

MS CONTIN  
(morphine extended-release tablets)

NUCYNTA ER  
(tapentadol extended-release)

OPANA ER  
(oxyronphine hydrochloride extended-release tablets)

OXYCONTIN  
(oxycodeinone hydrochloride extended-release tablet)

(Ttramadol hydrochloride extended-release)

TARGINIQ ER  
(oxycodeinone HCl/naloxone HCl extended-release tablets)

(Ttramadol hydrochloride extended-release)

TROXYCA ER  
(oxycodeinone hydrochloride/naltrexone extended-release capsules)

ULTRAM ER  
(tramadol hydrochloride extended-release)

VANTRELA ER  
(hydrocodone bitartrate extended-release tablets)

XTAMPZA ER  
(oxycodeinone extended-release capsules)

ZOHYDRO ER  
(hydrocodone bitartrate extended-release capsules)

Status: CVS Caremark Criteria
Type: Initial Step Therapy; Post Step Therapy Prior Authorization  Ref # 1360-D**

Please note that Xartemis XR is on a separate criteria.
*This criteria applies to both brand and generic, if available.
**1360-D may be used as a stand alone criteria OR in combination with Opioids ER Labeling Limit and Post Limit 1359-M or Opioids ER MME Limit and Post Limit 1361-M
FDA-APPROVED INDICATIONS
Arymo ER, Avinza, Kadian, MorphaBond, MS Contin, and Embeda

Arymo ER, Avinza, Kadian, MorphaBond, 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, 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, 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 risk of overdose and death with extended-release 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
ConZip is indicated for the management of moderate to moderately severe chronic pain in adults who require around-the-clock treatment of their pain for an extended period of time.

Dolophine Tablets
Dolophine 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 Dolophine 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 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.

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 of morphine daily, or at least 30 mg of oral oxycodone daily, or at least 8 mg of oral hydromorphone daily, 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 opioid analogues) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.

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/hour, 30 mg oral oxycodone/day, 8 mg oral hydromorphone/day, 25 mg oral oxymorphone/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 and Zohydro ER**

Hysingla ER and Zohydro ER (hydrocodone bitartrate) 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 Hysingla ER or 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.
• Hysingla ER and Zohydro ER are not indicated as an as-needed (prn) analgesic.

**Methadone Injection**

• For the treatment of moderate to severe pain not responsive to non-narcotic analgesics.
• For use in temporary treatment of opioid dependence in patients unable to take oral medication.

Outpatient maintenance and outpatient detoxification treatment may be provided only by opioid treatment programs (OTPs) certified by the Federal Substance Abuse and Mental Health Services Administration (SAMHSA) and registered by the Drug Enforcement Administration (DEA). This does not preclude the maintenance treatment of a patient with concurrent opioid addiction who is hospitalized for conditions other than opioid addiction and who requires temporary maintenance during the critical period of hospitalization, or of a patient whose enrollment has been verified in a program which has been certified for maintenance treatment with methadone.

**NOTE:** 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.

**Methadone Intensol**

Methadone Hydrochloride Intensol (oral concentrate) is indicated for the:

• Management of moderate to severe pain when a continuous, around-the-clock opioid analgesic is needed for an extended period of time
• 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 Hydrochloride Intensol (oral concentrate) is not for use:
• As an as-needed (prn) analgesic
• For pain that is mild or not expected to persist for an extended period of time
• For acute pain
• For postoperative pain

**Methadone Oral Solution**

Methadone Hydrochloride Oral Solution USP 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 USP 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 USP 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.

**Methadose Tablets**
Methadose Oral Tablets (methadone hydrochloride tablets USP) 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 Methadose 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.
- Methadose 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)).

**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 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 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**

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 orally or its equivalent.

**Limitations of Usage**

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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.

Tramadol Hydrochloride Extended-Release
Tramadol hydrochloride extended-release is indicated for the management of moderate to moderately severe chronic pain in adults who require around-the-clock treatment of their pain for an extended period of time.

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.

Ultram ER
Ultram 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.

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.
COVERAGE CRITERIA
Extended-release Opioid Analgesics will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for pain associated with cancer, 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.]
- AND
- The patient can safely take the requested dose based on their history of opioid use
  - OR
  - 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
  - The patient has severe continuous pain and has received an immediate release opioid for at least one week

Limits may apply.

RATIONALE
If the patient has filled a prescription for a ≥ 1 day supply of a drug indicating the patient is being treated for cancer within the past 365 days 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 in the past 365 days:
If the patient has filled a prescription for a ≥ 7 day supply of an immediate-release opioid agent within history in the past 90 days under a prescription benefit administered by CVS Caremark, then 1) when using this program in combination with Opioids ER Labeling Limit and Post Limit 1359-M or Opioids ER MME Limit and Post Limit 1361-M, the claim will proceed to the subsequent initial quantity limit criteria (1359-M or 1361-M) OR 2) 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 a ≥ 30 day supply of an extended-release opioid within the past 90 days under a prescription benefit administered by CVS Caremark, then 1) when using this program in combination with Opioids ER Labeling Limit and Post Limit 1359-M or Opioids ER MME Limit and Post Limit 1361-M, the claim will proceed to the subsequent initial quantity limit criteria (1359-M or 1361-M) 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 immediate-release opioid agent OR at least a 30 day supply of an extended-release opioid within 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 step therapy criteria will apply to the incoming prescription drug, and 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 using this program in combination with Opioids ER Labeling Limit and Post Limit 1359-M or Opioids ER MME Limit and Post Limit 1361-M, then subsequent initial quantity limits and post limits would apply.

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 in opioid-tolerant patients severe enough to require daily, around-the-clock, long-term opioid treatment in a patient who has been taking an opioid. 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.

The Centers for Disease Control and Prevention (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.  

Patients with chronic pain may need to be dosed on an around-the-clock basis rather than on an as needed basis. 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.  

National Comprehensive Cancer Network (NCCN) guidelines for Adult Cancer Pain recommend for continuous pain, to give pain medication on a regular schedule with supplemental doses for breakthrough pain. Add 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 every 1 hour as needed. The NCCN Palliative Care pain management recommendation is to treat according to NCCN guidelines for adult cancer pain management. Step therapy criteria and post limit quantities will not be set up for patients with cancer, a terminal condition or pain being managed through hospice or palliative care.

**PROGRAM DESCRIPTION**

This step therapy program applies to the following patients:
1) Patients requesting an extended-release opioid agent who have NOT tried and failed a 7 day supply of an immediate-release opioid agent within the past 90 days
2) Patients who have NOT been receiving an extended-release opioid agent for 30 days within the past 90 days
If the patient does not meet these initial step therapy criteria, then prior authorization is required.

If a patient has filled a 7 day supply of an immediate-release opioid agent within the past 90 days OR is has been receiving an extended-release opioid agent for 30 days within the past 90 days and is requesting the extended-release opioid agent for continuation of therapy, then the requested drug will be paid under the prescription benefit.

Step therapy criteria and post limit quantities will not be set up for patients with cancer, a terminal condition or pain being managed through hospice or palliative care.

**REFERENCES**

If the patient has filled a prescription for a ≥ 1 day supply of a drug indicating the patient is being treated for cancer within the past 365 days 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 in the past 365 days:
If the patient has filled a prescription for a ≥ 7 day supply of an immediate-release opioid agent within history in the past 90 days under a prescription benefit administered by CVS Caremark, then 1) when using this program in combination with
Opioids ER Labeling Limit and Post Limit 1359-M or Opioids ER MME Limit and Post Limit 1361-M, the claim will proceed to the subsequent initial quantity limit criteria (1359-M or 1361-M) OR 2) 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 a ≥ 30 day supply of an extended-release opioid within the past 90 days under a prescription benefit administered by CVS Caremark, then 1) when using this program in combination with Opioids ER Labeling Limit and Post Limit 1359-M or Opioids ER MME Limit and Post Limit 1361-M, the claim will proceed to the subsequent initial quantity limit criteria (1359-M or 1361-M) 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 immediate-release opioid agent OR at least a 30 day supply of an extended-release opioid within 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 step therapy criteria will apply to the incoming prescription drug, and 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 using this program in combination with Opioids ER Labeling Limit and Post Limit 1359-M or Opioids ER MME Limit and Post Limit 1361-M, then subsequent initial quantity limits and post limits would apply.

**CRITERIA FOR APPROVAL**

1. Is the requested drug being prescribed for pain associated with cancer, a terminal condition, or pain being managed through hospice or palliative care?  
   - Yes  
   - No  
   [If yes, then no further questions.]

2. Is the requested drug being prescribed for moderate to severe CHRONIC pain where use of an opioid analgesic is appropriate?  
   - Yes  
   - No  
   [Note: Chronic pain is generally defined as pain that typically lasts greater than 3 months.]

3. Can the patient safely take the requested dose based on their history of opioid use?  
   - Yes  
   - No

4. Is this request for continuation of therapy for a patient who has been receiving an extended-release opioid agent for at least 30 days?  
   - Yes  
   - No  
   [If yes, then no further questions.]

5. Does the patient have severe continuous pain and has the patient received an immediate release opioid for at least one week?  
   - Yes  
   - No

**Mapping Instructions**

<table>
<thead>
<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></td>
<td>Approve, 12 months Go to 2</td>
</tr>
</tbody>
</table>
| 2.  | Deny| Your plan covers this drug when you meet one of the following conditions:  
- You have moderate to severe chronic pain that requires opioids  
- You have pain due to cancer or a terminal condition  
- Your pain is being managed through hospice or palliative care  
Your use of this drug does not meet the requirement. This is based on the information we have. |
<p>| 3.  | Deny| Your plan covers this drug when you can safely take the drug based on your history of opioid use. Your use of this drug does not meet the requirement. This is based on the information we have. |
| 4.  |     | Approve, 12 Go to 5                         |</p>
<table>
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<td>Your plan covers this drug when you have one of these conditions:</td>
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<tr>
<td></td>
<td>- Pain due to cancer or a terminal condition</td>
</tr>
<tr>
<td></td>
<td>- Pain being managed through hospice or palliative care</td>
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<td></td>
<td>- You have already been taking an extended-release opioid drug for 30 days</td>
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<tr>
<td></td>
<td>- You have severe continuous pain and tried immediate-release opioids for one week</td>
</tr>
<tr>
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<td>Your use of this drug does not meet the requirement. This is based on the information we have.</td>
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</table>
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 indicated for the treatment of pulmonary arterial hypertension (PAH, WHO Group I) 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

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:
   - mPAP ≥ 25 mmHg
   - PCWP ≤ 15 mmHg
   - 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:
   - Post cardiac surgery
   - Chronic heart disease
   - Chronic lung disease associated with prematurity
   - Congenital diaphragmatic hernia

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with PAH who are currently receiving Opsumit therapy through a paid pharmacy or medical benefit.

IV. APPENDIX

WHO Classification of Pulmonary Hypertension

WHO Group 1. Pulmonary Arterial Hypertension (PAH)

1.1 Idiopathic (IPAH)

1.2 Heritable PAH

1.2.1 Germline mutations in the bone morphogenetic protein receptor type 2 (BMPR2)
1.2.2 Activin receptor-like kinase type 1 (ALK1), endoglin (with or without hereditary hemorrhagic telangiectasia), Smad 9, caveolin-1 (CAV1), potassium channel super family K member-3 (KCNK3)
1.2.3 Unknown
1.3 Drug- and toxin-induced
1.4. 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’. Pulmonary veno-occlusive disease (PVOD) and/or pulmonary capillary hemangiomatosis (PCH)
1”. Persistent pulmonary hypertension of the newborn (PPHN)

WHO Group 2. Pulmonary Hypertension Owing to Left Heart Disease
2.1 Systolic dysfunction
2.2 Diastolic dysfunction
2.3 Valvular disease
2.4 Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies

WHO Group 3. Pulmonary Hypertension Owing to Lung Disease and/or Hypoxia
3.1 Chronic obstructive pulmonary disease
3.2 Interstitial lung disease
3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
3.4 Sleep-disordered breathing
3.5 Alveolar hypoventilation disorders
3.6 Chronic exposure to high altitude
3.7 Developmental abnormalities

WHO Group 4. Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

WHO Group 5. Pulmonary Hypertension with Unclear Multifactorial Mechanisms
5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders, splenectomy
5.2 Systemic disorders: sarcoidosis, pulmonary Langerhans cell histiocytosis: lymphangioleiomyomatosis, neurofibromatosis, vasculitis
5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
5.4 Others: tumoral obstruction, fibrosing mediastinitis, chronic renal failure on dialysis, segmental PH

V. REFERENCES
PRIOR AUTHORIZATION CRITERIA

BRAND NAME*  
(generic) ORALAIR  
(Sweet Vernal, Orchard, Perennial Rye, Timothy, and Kentucky Blue Grass Mixed Pollens Allergen Extract)

Status: CVS Caremark Criteria  
Type: Initial Prior Authorization  
MDC-1  
Ref # 1132 -A

* Drugs that are listed in the target drug box include both brand and generic and all dosages forms and strengths unless otherwise stated

FDA-APPROVED INDICATIONS
Oralair is an allergen extract indicated as immunotherapy for the treatment of grass pollen-induced allergic rhinitis with or without conjunctivitis confirmed by positive skin test or in vitro testing for pollen-specific IgE antibodies for any of the five grass species contained in this product. Oralair is approved for use in persons 10 through 65 years of age. Oralair is not indicated for the immediate relief of allergy symptoms.

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 grass pollen-induced allergic rhinitis, with or without conjunctivitis, confirmed by positive skin test or in vitro testing for pollen-specific IgE antibodies for any of the five grass species contained in this product.

 AND

- The patient does not have any of the following: severe, unstable or uncontrolled asthma, history of any severe systemic allergic reaction or any severe local reaction to sublingual allergen immunotherapy, history of eosinophilic esophagitis, medical conditions that may reduce the ability of the patient to survive a serious allergic reaction or increase the risk of adverse reactions after epinephrine administration and is not on any medication(s) that can inhibit or potentiate the effect of epinephrine.

 AND

- The requested drug is being prescribed by or in consultation with an allergist/immunologist.

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.

Oralair is an allergen extract indicated as immunotherapy for the treatment of grass pollen-induced allergic rhinitis with or without conjunctivitis confirmed by positive skin test or in vitro testing for pollen-specific IgE antibodies for any of the five grass species contained in this product. Oralair is approved for use in persons 10 through 65 years of age. Oralair is not indicated for the immediate relief of allergy symptoms.

Oralair may not be suitable for patients with certain medical conditions that may reduce the ability to survive a serious allergic reaction or increase the risk of adverse reactions after epinephrine administration. Examples of these medical

Ora

conditions include but are not limited to: markedly compromised lung function (either chronic or acute), unstable angina, recent myocardial infarction, significant arrhythmia, and uncontrolled hypertension.

Oralair may not be suitable for patients who are taking medications that can potentiate or inhibit the effect of epinephrine. These medications include beta-adrenergic blockers, alpha-adrenergic blockers, ergot alkaloids, tricyclic antidepressants, levothyroxine sodium, monoamine oxidase inhibitors, the antihistamines chlorpheniramine and diphenhydramine, cardiac glycosides, and diuretics.

Oralair is contraindicated in the following conditions: severe, unstable or uncontrolled asthma, history of any severe systemic allergic reaction or any severe local reaction to sublingual allergen immunotherapy, and a history of eosinophilic esophagitis.

REFERENCES

Written by: Specialty Clinical Development (ST)
Date Written: 04/2014
Revised: KF 02/2015, UM development SF 03/2015 (changed to non specialty), 03/2016 (no clinical changes), (SE) 06/2016 (created separate Med D), (SF) 03/2017
Reviewed: CDPR/KP 04/2014, SES 12/2014 (KRU) 03/2015; (JG) 03/2017
04/2014, 12/2014, 06/2015, 06/2016, 06/2017

CRITERIA FOR APPROVAL

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Guidelines for Approval

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<th>Duration of Approval</th>
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</tr>
<tr>
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<tr>
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<td>2</td>
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<tr>
<td>Yes</td>
<td>No</td>
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</tbody>
</table>
| 1. Go to 2   | Deny       | Your plan covers this drug when it is being used for the following: -immunotherapy for grass pollen-induced allergic rhinitis confirmed by positive skin test or *in vitro* testing for pollen-specific IgE antibodies for any of the 5 grass species (Sweet Vernal, Orchard, Perennial Rye, Timothy, Kentucky Blue Grass)  
Your use of this drug does not meet the requirements. This is based on the information we have. |
| 2. Deny      | Go to 3    | Your plan covers this drug when you do not have one of these conditions:  
 - Severe, unstable, or uncontrolled asthma  
 - History of any severe systemic allergic reaction or any severe local reaction to sublingual allergen immunotherapy  
 - A history of eosinophilic esophagitis  
 - Medical conditions that may reduce the ability of the patient to survive a serious allergic reaction or increase the risk of adverse reactions after epinephrine administration  
 - Patient is on any medication(s) that can inhibit or potentiate the effect of epinephrine  
Your use of this drug does not meet the requirements. This is based on the information we have. |
| 3. Approve, 6 months | Deny       | Your plan covers this drug when it is prescribed by or working with an allergist/immunologist. Your use of this drug does not meet the requirements. This is based on the information we have. |
## PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>ORAL/INTRANASAL FENTANYL PRODUCTS</th>
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<tbody>
<tr>
<td>BRAND NAME*</td>
<td>(generic)</td>
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</tbody>
</table>

- **ABSTRAL** (fentanyl citrate sublingual tablet)
- **ACTIQ** (fentanyl citrate oral transmucosal lozenge)
- **FENTORA** (fentanyl citrate buccal tablet)
- **LAZANDA** (fentanyl nasal spray)
- **ONSOlis** (fentanyl buccal soluble film)
- **SUBSYS** (fentanyl sublingual spray)

*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

**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 opioid therapy for their underlying persistent cancer pain. Patients must remain on around-the-clock opioids when taking Abstral. Abstral is contraindicated for patients who are not already tolerant to opioids because life-threatening respiratory depression and death could result at any dose in patients not on a chronic regimen of opioids. For this reason, Abstral is contraindicated in the management of acute or postoperative pain, including headache/migraine, dental pain, or use in the emergency room. Abstral is intended to be prescribed only by healthcare professionals who are knowledgeable of, and skilled in, the use of Schedule II opioids to treat 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. Patients must remain on around-the-clock opioids when taking Actiq. This product must not be used in opioid non-tolerant patients because life-threatening respiratory depression and death could occur at any dose in patients not on a chronic regimen of opioids. For this reason, Actiq is contraindicated in the management of acute or postoperative pain, including headache/migraine, and dental 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. Patients must remain on around-the-clock opioids while taking Fentora. Fentora should not be used in opioid non-tolerant patients. Fentora should not be used in the management of acute or postoperative pain, including headache/migraine, and dental 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 opioid therapy for their underlying persistent cancer pain. Patients must remain on around-the-clock opioids when taking Lazanda. Lazanda is contraindicated for patients who are not already tolerant to opioids because life-threatening respiratory depression and death could occur in patients not taking chronic opioids. For this reason, Lazanda is contraindicated in the management of acute or postoperative pain, including headache/migraine, or dental pain. Lazanda is intended to be prescribed only by healthcare professionals who are knowledgeable of and skilled in the use of Schedule II opioids to treat cancer pain.

Onsolis
Onsolis (fentanyl buccal soluble film) is an opioid analgesic 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 opioid therapy for their underlying persistent cancer pain. Patients must remain on around-the-clock opioids while taking Onsolis. This product must not be used in opioid non-tolerant patients because life-threatening respiratory depression could occur in patients not taking chronic opiates. For this reason, Onsolis is contraindicated in the management of acute or postoperative pain, including headache/migraine, dental pain, or use in the emergency room.

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. Patients must remain on around-the-clock opioids when taking Subsys. This product must not be used in opioid non-tolerant patients because life-threatening respiratory depression and death could occur at any dose in patients not on a chronic regimen of opioids. For this reason, Subsys is contraindicated in the management of acute or postoperative pain, including headache/migraine, dental pain, or in the emergency room.

For All Oral/Intranasal Fentanyl Products:
Patients considered opioid tolerant are those who are taking at least: 60 mg oral morphine/day, 25 mcg transdermal fentanyl/hour, 30 mg oral oxycodone/day, 8 mg oral hydromorphone/day, 25 mg oral oxymorphone/day, or an equianalgesic dose of another opioid for one week or longer.

Oral/Intranasal Fentanyl Products are intended to be used only in the care of cancer patients and only by oncologists and pain specialists who are knowledgeable of and skilled in the use of Schedule II opioids to treat cancer pain.

Limitations of Use:
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 patient has CANCER related pain. This drug is indicated for the treatment of breakthrough CANCER related pain only. Prescriber must submit chart notes or other documentation supporting a diagnosis of cancer related pain and list type of cancer AND
- Chart notes or other documentation supporting a diagnosis of cancer related pain have been submitted to CVS Health by fax AND

Oral-Intranasal Fentanyl Products.docx ©2017 CVS Caremark. All rights reserved.

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• The 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 AND
• The patient can safely take the requested dose based on their history of opioid use AND
• If additional quantities are being requested, then:
  o The patient’s dose of a concomitant long-acting analgesic is being increased OR
  o 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

Quantity Limit applies.

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 ONLY for the management of breakthrough pain in cancer patients who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain. Patients considered opioid tolerant are those who are taking at least: 60 mg oral morphine per day, 25 mcg transdermal fentanyl per hour, 30 mg of oral oxycodone per day, 8 mg oral hydromorphone per day, 25 mg oral oxymorphone per day or an equianalgesic dose of another opioid for one week or longer. Due to the risk of respiratory depression, Abstral, Actiq, Fentora, Lazanda, Onsolis, and Subsys are contraindicated in opioid non-tolerant patients.

Due to differences in pharmacokinetic properties and individual variability, patients cannot be switched on a mcg per mcg basis from one fentanyl product to another. Oral/intranasal fentanyl products are not equivalent on a mcg per mcg basis. 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. Dose titration should be done if the patient requires more than 1 dose/breakthrough pain episode for several consecutive episodes. Patients experiencing >4 breakthrough pain episodes/day should have the dose of their long-term opioid re-evaluated.7

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 25 days or 90 bottles per 75 days will be placed on the Lazanda products since each container 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), Subsys 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg, Onsolis 200 mcg, 400 mcg, 600 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, Abstral 800 mcg, Lazanda 300 mcg or 400 mcg, Onsolis 800 mcg, or Onsolis 1200 mcg is only provided up to 4 units (Abstral, Onsolis) or 8 sprays (Lazanda) per day to avoid exceeding the labeled maximum dose.

REFERENCES

Oral-Intranasal Fentanyl Products.docx  ©2017 CVS Caremark. All rights reserved.

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### CRITERIA FOR APPROVAL

1. **This drug is indicated for the treatment of breakthrough CANCER related pain only. Does the patient have CANCER related pain?**
   - Yes
   - No

   If yes, 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 by fax?**
   - Yes
   - No

   [Tech Note: MUST obtain a physical copy of chart notes or other documentation supporting a diagnosis of cancer related pain AND verify that prescriber has listed type of cancer. If the PA is worked over the phone, then the prescriber MUST fax in 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. **Is the 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?**
   - Yes
   - No

4. **Can the patient safely take the requested dose based on their history of opioid use?**
   - Yes
   - No

5. **Which drug is being requested? Please check drug being requested.**
   - Abstral 600 mcg or 800 mcg (if checked, then go to 6)
   - Abstral 100 mcg, 200 mcg, 300 mcg, 400 mcg (if checked, then go to 8)
   - Actiq (all strengths) (if checked, then go to 8)
   - Fentora (all strengths) (if checked, then go to 8)
   - Onsolis 200 mcg, 400 mcg, 600 mcg (if checked, then go to 8)
   - Onsolis 800 mcg or 1200 mcg (if checked, then go to 6)
   - Lazanda 100 mcg (if checked, then go to 9)
   - Lazanda 300 mcg or 400 mcg (if checked, then go to 7)
   - Subsys 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg (if checked, then go to 8)
   - Subsys 1200 mcg, 1600 mcg (if checked, then go to 10)

6. **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?**
   - Yes
   - No

   [No further questions.]

   [Tech 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.]

7. **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?**
   - Yes
   - No

   [No further questions.]

   [Tech 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.]
<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>8  Coverage is provided for up to 120 units per month of the following:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>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, 800 mcg, If higher quantities are needed, 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 11.]</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>9  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, 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 11.]</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>10 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, 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.]</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>11 Is the patient's dose of a concomitant long-acting analgesic being increased? [If yes, then skip to question 13.]</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>12 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.] [Tech Note: 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., 30 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.]</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>13 Which drug is being requested? Please check drug being requested.</td>
<td></td>
<td></td>
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<tr>
<td>[] Abstral 100 mcg, 200 mcg, 300 mcg, 400 mcg (if checked, then go to 14)</td>
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<td></td>
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<tr>
<td>[] Actiq (all strengths) (if checked, then go to 14)</td>
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<tr>
<td>[] Fentora (all strengths) (if checked, then go to 14)</td>
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<td></td>
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<tr>
<td>[] Onsolis 200 mcg, 400 mcg, 600 mcg (if checked, then go to 14)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>[] Lazanda 100 mcg (if checked, then go to 15)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>[] Subsys 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg (if checked, then go to 14)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>[] Subsys 1200 mcg, 1600 mcg (if checked, then go to 16)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14 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, 800 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.]</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>
15 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.]

16 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?  
[Note Subsys packaging: Supplied as 2 sprays per blister for Subsys 1200 mcg and 1600 mcg.]

Mapping Instructions

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
<th>DENIAL REASONS – DO NOT USE FOR MEDICARE PART D</th>
</tr>
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<tbody>
<tr>
<td>1.</td>
<td>Go to 2</td>
<td>Deny</td>
</tr>
<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>1=6; 2=8; 3=8; 4=8; 5=8; 6=6; 7=9; 8=7; 9=8; 10=10</td>
<td>N/A</td>
</tr>
<tr>
<td>6.</td>
<td>Deny</td>
<td>Approve, 12 months</td>
</tr>
<tr>
<td>7.</td>
<td>Deny</td>
<td>Approve, 12 months</td>
</tr>
</tbody>
</table>

You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:
- 120 units per month of Abstral 600 mcg, 800 mcg
- 120 units per month of Onsolis 800 mcg, 1200 mcg
You have been approved for the maximum quantity that your plan covers. Your request for additional quantities of the requested drug and strength has been denied.

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
<p>| | | |</p>
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<tbody>
<tr>
<td>8.</td>
<td>Go to 11</td>
<td>Approve, 12 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>120 units per 25 days OR 360 units per 75 days* of:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Abstral 100 mcg, 200 mcg, 300 mcg, 400 mcg</td>
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<tr>
<td></td>
<td></td>
<td>Actiq (all strengths)</td>
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<tr>
<td></td>
<td></td>
<td>Fentora (all strengths)</td>
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<tr>
<td></td>
<td></td>
<td>Onsolis 200 mcg, 400 mcg, 600 mcg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Subsys 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg</td>
</tr>
<tr>
<td>9.</td>
<td>Go to 11</td>
<td>Approve, 12 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30 bottles per 25 days or 90 bottles per 75 days* of:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lazanda 100 mcg</td>
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<tr>
<td>10.</td>
<td>Go to 11</td>
<td>Approve, 12 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>240 sprays (i.e., 120 blisters) per 25 days or 720 sprays (i.e., 360 blisters) per 75 days* of Subsys 1200 mcg or 1600 mcg</td>
</tr>
<tr>
<td>11.</td>
<td>Go to 13</td>
<td>Go to 12</td>
</tr>
<tr>
<td>12.</td>
<td>Go to 13</td>
<td>Deny</td>
</tr>
<tr>
<td></td>
<td></td>
<td>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:</td>
</tr>
<tr>
<td></td>
<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>
</tr>
<tr>
<td></td>
<td></td>
<td>- 240 sprays per month (i.e., 30 bottles per month) of Lazanda 100 mcg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- 240 sprays per month (i.e., 120 blisters per month) of Subsys 1200 mcg or 1600 mcg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>You have been approved for the maximum quantity that your plan covers. Your request for additional quantities of the requested drug and strength has been denied.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Your plan covers additional quantities of this drug when you meet one of these conditions:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- The dose of your long-acting opioid drug is being increased</td>
</tr>
<tr>
<td></td>
<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>
</tr>
<tr>
<td></td>
<td></td>
<td>Your use of this drug does not meet the requirement. This is based on the information we have.</td>
</tr>
<tr>
<td>13.</td>
<td></td>
<td>1=14; 2=14; N/A</td>
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<tr>
<td>14.</td>
<td>Deny</td>
<td>Approve, 12 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>180 units per 25 days OR 540 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</td>
</tr>
<tr>
<td>15.</td>
<td>Deny</td>
<td>Approve, 12 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>45 bottles per 25 days or 135 bottles per 75 days* of: Lazanda 100 mcg</td>
</tr>
<tr>
<td>16.</td>
<td>Deny</td>
<td>Approve, 12 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>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</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
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 severly 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:
      - mPAP ≥ 25 mmHg
      - PCWP ≤ 15 mmHg
      - 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:
      - Post cardiac surgery
      - Chronic heart disease
      - Chronic lung disease associated with prematurity
      - Congenital diaphragmatic hernia

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with PAH who are currently receiving Orenitram therapy through a paid pharmacy or medical benefit.

IV. APPENDIX

WHO Classification of Pulmonary Hypertension
WHO Group 1. Pulmonary Arterial Hypertension (PAH)
1.1 Idiopathic (IPAH)
1.2 Heritable PAH
   1.2.1 Germline mutations in the bone morphogenetic protein receptor type 2 (BMPR2)
   1.2.2 Activin receptor-like kinase type 1 (ALK1), endoglin (with or without hereditary hemorrhagic telangiectasia), Smad 9, caveolin-1 (CAV1), potassium channel super family K member-3 (KCNK3)
1.2.3 Unknown
1.3 Drug- and toxin-induced
1.4. 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'. Pulmonary veno-occlusive disease (PVOD) and/or pulmonary capillary hemangiomatosis (PCH)
1". Persistent pulmonary hypertension of the newborn (PPHN)

WHO Group 2. Pulmonary Hypertension Owing to Left Heart Disease
2.1 Systolic dysfunction
2.2 Diastolic dysfunction
2.3 Valvular disease
2.4 Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies

WHO Group 3. Pulmonary Hypertension Owing to Lung Disease and/or Hypoxia
3.1 Chronic obstructive pulmonary disease
3.2 Interstitial lung disease
3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
3.4 Sleep-disordered breathing
3.5 Alveolar hypoventilation disorders
3.6 Chronic exposure to high altitude
3.7 Developmental abnormalities

WHO Group 4. Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

WHO Group 5. Pulmonary Hypertension with Unclear Multifactorial Mechanisms
5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders, splenectomy
5.2 Systemic disorders: sarcoidosis, pulmonary Langerhans cell histiocytosis: lymphangioleiomyomatosis, neurofibromatosis, vasculitis
5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
5.4 Others: tumoral obstruction, fibrosing mediastinitis, chronic renal failure on dialysis, segmental PH

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

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 received Otezla or any biologic disease-modifying antirheumatic drug (DMARD) indicated for the treatment of moderate to severe plaque psoriasis in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Otezla.

   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, genital/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)
   1. Authorization of 24 months may be granted for members who have received Otezla in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Otezla.

   2. Authorization of 24 months may be granted for treatment of active psoriatic arthritis when any of the following criteria is met:
      a. Member has had an inadequate response to at least a 3-month trial of at least one prior biologic DMARD indicated for PsA (see Appendix B).
      b. Member has experienced an intolerance or adverse event to a trial of at least one prior biologic DMARD indicated for PsA.
      c. All biologic DMARDs indicated for PsA are not appropriate for the member (e.g., due to comorbidities or a history of infections contraindicating any biologic DMARD).
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. 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 (male or female)
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

Appendix B: Biologic DMARDs Indicated for Psoriatic Arthritis
1. Cimzia® (certolizumab pegol)
2. Cosentyx® (secukinumab)
3. Enbrel® (etanercept)
4. Humira® (adalimumab)
5. Remicade® (infliximab)
6. Simponi® (golimumab)
7. Stelara® (ustekinumab)

V. 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.

B. Compendial Uses

1. Chronic myelogenous leukemia
2. Myeloproliferative neoplasm (primary myelofibrosis and post-polycythemia vera or post-essential thrombocytemia myelofibrosis)

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. Chronic myelogenous leukemia (CML)
   Authorization of 12 months may be granted for the treatment of CML.

D. Myeloproliferative neoplasm
   Authorization of 12 months may be granted for the treatment of myeloproliferative neoplasm (primary myelofibrosis and post-polycythemia vera or post-essential thrombocytemia 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

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 HER2-positive breast cancer

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

II. CRITERIA FOR INITIAL APPROVAL

   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

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 Indications
   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
   Systemic light chain amyloidosis

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.

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 Indication
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)
Authorization of 12 months may be granted for treatment of metastatic squamous NSCLC when Portrazza is used in combination with gemcitabine and cisplatin.

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

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

Praluent is indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease, who require additional lowering of low density lipoprotein cholesterol (LDL-C).

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 for members who meet ALL of the criteria listed below:

1. Member has a history of clinical ASCVD (See Appendix A).
2. Member meets at least ONE of the following requirements [a or b]:
   a. Member has a current LDL-C level ≥ 70 mg/dL after at least three months of treatment with a high-intensity statin dose (e.g., atorvastatin ≥ 40 mg or rosuvastatin ≥ 20 mg daily) plus ezetimibe 10 mg daily. If the member is unable to tolerate a high-intensity statin dose, a moderate-intensity statin dose (e.g., atorvastatin 20 mg or equivalent) 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. Heterozygous Familial Hypercholesterolemia (HeFH)

Authorization of 12 months may be granted for members who meet ALL of the criteria listed below:

1. Member has a diagnosis of familial hypercholesterolemia (See Appendix D).
2. Member meets at least ONE of the following requirements [a, b, c or d]:
   a. With ASCVD: See Section A.
   b. Without ASCVD: Member has a current LDL-C level ≥ 100 mg/dL after at least three months of treatment with a high-intensity statin dose (i.e., atorvastatin ≥ 40 mg or rosuvastatin ≥ 20 mg daily) plus ezetimibe 10 mg daily.
   c. Member has a current LDL-C level ≥ 100 mg/dL with contraindication or intolerance to statins (See Appendices B and C) and is taking ezetimibe 10mg daily.
   d. Member has a current LDL-C level ≥ 100 mg/dL and contraindication to both statins and ezetimibe (See Appendix C).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members who have received Praluent through a pharmacy or medical benefit and who achieve or maintain an LDL-C reduction (e.g., LDL-C is now at goal, robust lowering of LDL-C).
IV. 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
- Intolerable SAMS persisting at least two weeks, which subsided when the medication was discontinued, and reemerged with a statin re-challenge.
  NOTE: Re-challenge must be with a different statin.
- Statin-associated elevation in CK level \( \geq 10 \) times upper limit of normal (ULN)
  NOTE: Statin re-challenge is NOT required for members who have experienced an elevation of CK level greater than or equal to 10 times ULN after receiving lipid-lowering therapy (LLT) with a statin.

APPENDIX C. Contraindications to statins and ezetimibe
- Contraindications to statins
  o Active liver disease, including unexplained persistent elevations in hepatic transaminase levels (e.g., alanine transaminase (ALT) level \( \geq 3 \) times ULN)
  o Women who are pregnant or may become pregnant
  o Nursing mothers
- Contraindication to ezetimibe
  o Hypersensitivity reactions (e.g., anaphylaxis, angioedema, rash and urticaria)

APPENDIX D: 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

V. 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. Metastatic renal cell carcinoma in adults
   2. Metastatic melanoma in adults

B. Compendial Uses
   1. Relapsed or stage IV surgically unresectable kidney cancer with clear cell histology
   2. Metastatic or unresectable melanoma

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. Melanoma
   Authorization of 12 months may be granted for treatment of metastatic or unresectable melanoma.

III. CONTINUATION OF THERAPY

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

IV. REFERENCES


DOCUMENT HISTORY
Written: Specialty Clinical Development (AK) 02/2007

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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. 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. Severe aplastic anemia
   Authorization of 6 months may be granted to members for the treatment of severe aplastic anemia.

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. Severe 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.

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.

A. FDA-Approved Indication

Pulmozyme is indicated for daily administration in conjunction with standard therapies for the management of cystic fibrosis patients to improve pulmonary function.

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 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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<tr>
<th>BRAND NAME</th>
<th>QSYMIA (generic) (phentermine and topiramate extended-release)</th>
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**Status:** CVS Caremark Criteria  
**Type:** Initial Prior Authorization  
Ref # 794-A

**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**

Qsymia 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 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 medication 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 use of Qsymia can cause fetal harm and weight loss offers no potential benefit to a pregnant woman. Available epidemiologic data indicate an increased risk in oral clefts with first-trimester exposure to topiramate, a component of Qsymia. When multiple species of pregnant animals received topiramate at clinically relevant doses, structural malformations, including craniofacial defects, and reduced fetal weights occurred in offspring. If this drug is used during pregnancy, or if a patient becomes pregnant while taking this drug, treatment should be discontinued immediately and the patient should be apprised of the potential hazard to a fetus. There is a Qsymia Pregnancy Surveillance Program to monitor maternal-fetal outcomes of pregnancies that occur during Qsymia therapy. Because of the teratogenic risk...
associated with Qsymia therapy, Qsymia is available through a limited program under the REMS. Under the Qsymia REMS, only certified pharmacies may distribute Qsymia.

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 ≥ 30 kg/m² or ≥ 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.

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
CRITERIA FOR APPROVAL

1. Has the patient completed at least 12 weeks of Qsymia 15 mg/92 mg therapy?  
   [If yes, then skip to question 4.]  
   Yes No

2. 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

3. Did the patient lose at least 3 percent of baseline body weight or will the patient’s dose be escalated?  
   [No further questions required.]  
   Yes No

4. Did the patient lose at least 5 percent of baseline body weight or has the patient continued to maintain their weight loss?  
   [No further questions required.]  
   Yes No

5. 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

6. 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

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

Guidelines for Approval

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Mapping Instructions

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DENIAL REASONS – DO NOT USE FOR MEDICARE PART D

- Your plan covers this drug when you meet one of these conditions:
  - You have lost at least 3 percent of your body weight
  - If you did not lose at least 3 percent of your body weight, then you will take a higher dose
  Your use of this drug does not meet the requirements. This is based on the information we have.

- Your plan covers this drug when you have lost at least 5 percent of your body weight or have continued to keep your weight loss off. Your use of this drug does not meet the requirement. This is based on the information we have.
- 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 use of this drug does not meet the requirements. This is based on the information we have.

| 7. Approve for 3 months | Deny | Your plan covers this drug when you will diet and exercise. Your use of this drug does not meet the requirement. This is based on the information we have. |
PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

RAGWITEK
(short ragweed pollen allergen extract)

Status: CVS Caremark Criteria
Type: Initial 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

FDA-APPROVED INDICATIONS
Ragwitek is an allergen extract indicated as immunotherapy for the treatment of short ragweed pollen-induced allergic rhinitis with or without conjunctivitis confirmed by positive skin test or in vitro testing for pollen-specific IgE antibodies for short ragweed pollen. Ragwitek is approved for use in persons 18 through 65 years of age. Ragwitek is not indicated for the immediate relief of allergic symptoms.

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 short ragweed pollen-induced allergic rhinitis, with or without conjunctivitis, confirmed by positive skin test or in vitro testing for pollen-specific IgE antibodies for short ragweed pollen.
  AND
- The patient does not have any of the following: severe, unstable or uncontrolled asthma, history of any severe systemic allergic reaction or any severe local reaction to sublingual allergen immunotherapy, history of eosinophilic esophagitis, medical conditions that may reduce the ability of the patient to survive a serious allergic reaction or increase the risk of adverse reactions after epinephrine administration and is not on any medication(s) that can inhibit or potentiate the effect of epinephrine
  AND
- The requested drug is being prescribed by or in consultation with an allergist/immunologist

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.

Effective management of allergic rhinitis may require combinations of aggressive avoidance measures (eg, avoidance of rhinitis triggers, limiting outdoor exposure when high pollen counts are present), medications, management of coexisting conditions, and/or allergen immunotherapy. A wide range of oral and intranasal pharmacologic treatments exists consisting of antihistamines, decongestants, corticosteroids, cromolyn, anticholinergics, anti-leukotriene agents, and nasal saline.

Ragwitek is an allergen extract indicated as immunotherapy for the treatment of short ragweed pollen-induced allergic rhinitis with or without conjunctivitis confirmed by positive skin test or in vitro testing for pollen-specific IgE antibodies for short ragweed pollens. Ragwitek is approved for use in persons 18 through 65 years of age. Ragwitek is not indicated for the immediate relief of allergic symptoms.
Ragwitek may not be suitable for patients with certain medical conditions that may reduce the ability to survive a serious allergic reaction or increase the risk of adverse reactions after epinephrine administration. Examples of these medical conditions include but are not limited to: markedly compromised lung function (either chronic or acute), unstable angina, recent myocardial infarction, significant arrhythmia, and uncontrolled hypertension.

Ragwitek may not be suitable for patients who are taking medications that can potentiate or inhibit the effect of epinephrine. These medications include beta-adrenergic blockers, alpha-adrenergic blockers, ergot alkaloids, tricyclic antidepressants, levothyroxine sodium, monoamine oxidase inhibitors, the antihistamines chlorpheniramine and diphenhydramine, cardiac glycosides, and diuretics.

Ragwitek is contraindicated in the following conditions: severe, unstable or uncontrolled asthma, history of any severe systemic allergic reaction or any severe local reaction to sublingual allergen immunotherapy, and a history of eosinophilic esophagitis.

REFERENCES
## Guidelines for Approval

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### Mapping Instructions

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| 1. Go to 2 | Deny | Your plan covers this drug when it is being used for the following:
| | | -- immunotherapy for short ragweed pollen-induced allergic rhinitis confirmed by positive skin test or in vitro testing for pollen-specific IgE antibodies for short ragweed pollen? |
| | | Your use of this drug does not meet the requirements. This is based on the information we have. |
| 2. Deny | Go to 3 | Your plan covers this drug when you do not have one of these conditions:
| | | — Severe, unstable, or uncontrolled asthma |
| | | — History of any severe systemic allergic reaction or any severe local reaction to sublingual allergen immunotherapy |
| | | — A history of eosinophilic esophagitis |
| | | — Medical conditions that may reduce the ability of the patient to survive a serious allergic reaction or increase the risk of adverse reactions after epinephrine administration |
| | | — Patient is on any medication(s) that can inhibit or potentiate the effect of epinephrine |
| | | Your use of this drug does not meet the requirements. This is based on the information we have. |
| 3. Approve, 6 months | Deny | Your plan covers this drug when it is prescribed by or with an allergist. Your use of this drug does not meet the requirements. This is based on the information we have. |
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

A. RA and pJIA
   Authorization of 24 months may be granted for members who meet ANY of the following criteria:
   1. Member has tried and had an inadequate response or intolerance to generic methotrexate.
   2. Member has an inability to prepare and administer generic injectable methotrexate.

B. Psoriasis
   Authorization of 24 months may be granted for members who meet BOTH of the following criteria:
   1. Member has tried and had an inadequate response or intolerance to generic oral methotrexate.
   2. 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

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 to decrease the frequency of clinical exacerbations and delay the accumulation of physical disability.

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 24 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 24 months may be granted to members for the treatment of a first clinical episode of 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

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 actretin (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).
Note: Members who have received Remicade, Inflectra, Renflexis 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 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


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 as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease, who require additional lowering of low density lipoprotein cholesterol (LDL-C).

B. 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 are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Clinical atherosclerotic cardiovascular disease (ASCVD)
Authorization of 12 months may be granted for members who meet ALL of the criteria listed below:
1. Member has a history of clinical ASCVD (See Appendix A).
2. Member meets at least ONE of the following requirements [a or b]:
   a. Member has a current LDL-C level ≥ 70 mg/dL after at least three months of treatment with a high-intensity statin dose (e.g., atorvastatin ≥ 40 mg or rosuvastatin ≥ 20 mg daily) plus ezetimibe 10 mg daily. If the member is unable to tolerate a high-intensity statin dose, a moderate-intensity statin dose (e.g., atorvastatin 20 mg or equivalent) 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. Heterozygous Familial Hypercholesterolemia (HeFH)
Authorization of 12 months may be granted for members who meet ALL of the criteria listed below:
1. Member has a diagnosis of familial hypercholesterolemia (See Appendix D).
2. Member meets at least ONE of the following requirements [a, b, c or d ]:
   a. With ASCVD: See Section A.
   b. Without ASCVD: Member has a current LDL-C level ≥ 100 mg/dL after at least three months of treatment with a high-intensity statin dose (i.e., atorvastatin ≥ 40 mg or rosuvastatin ≥ 20 mg daily) plus ezetimibe 10 mg daily.
   c. Member has a current LDL-C level ≥ 100 mg/dL with contraindication or intolerance to statins (See Appendices B and C) and is taking ezetimibe 10mg daily.
   d. Member has a current LDL-C level ≥ 100 mg/dL and contraindication to both statins and ezetimibe (See Appendix C).
C. **Homozygous Familial Hypercholesterolemia FH**

Authorization for 12 months may be granted for members who meet ALL of the applicable criteria listed below:

1. Member has a diagnosis of homozygous FH confirmed by genetic analysis or clinical criteria (See Appendix E).
2. Member meets at least ONE of the following requirements [a, b, c, d, e or f]:
   a. With ASCVD: See Section A.
   b. Without ASCVD: Member has a current LDL-C level ≥ 100 mg/dL after at least three months of treatment with a high-intensity statin dose (i.e., atorvastatin ≥ 40 mg or rosuvastatin ≥ 20 mg daily) plus ezetimibe 10 mg daily.
   c. Member has a current LDL-C level ≥ 100 mg/dL with a contraindication or intolerance to statins (See Appendices B and C) and is receiving ezetimibe 10 mg daily.
   d. Member has a current LDL-C level ≥ 100 mg/dL and a contraindication to both statins and ezetimibe (See Appendix C).
   e. Member has received Juxtapid or Kynamro through a prior authorization process of a pharmacy or medical benefit.
   f. Member has been treated regularly with lipid apheresis within the previous 3 months.

III. **CONTINUATION OF THERAPY**

Authorization of 12 months may be granted for members who have received Repatha through a pharmacy or medical benefit and who achieve or maintain an LDL-C reduction (e.g., LDL-C is now at goal, robust lowering of LDL-C).

IV. **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**

- Intolerable SAMS persisting at least two weeks, which subsided when the medication was discontinued, and reemerged with a statin re-challenge.
  
  **NOTE:** Re-challenge must be with a different statin.

  **NOTE:** Statin re-challenge is NOT required for members who have experienced an elevation of CK level greater than or equal to 10 times ULN after receiving lipid-lowering therapy (LLT) with a statin.

**APPENDIX C. Contraindications to statins and ezetimibe**

- Contraindications to statins
  - Active liver disease, including unexplained persistent elevations in hepatic transaminase levels (e.g., alanine transaminase (ALT) level ≥ 3 times ULN)
  - Women who are pregnant or may become pregnant
Nursing mothers
- Contraindication to ezetimibe
  - Hypersensitivity reactions (e.g., anaphylaxis, angioedema, rash and urticaria)

APPENDIX D: 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

APPENDIX E: Diagnosis of Homozygous FH
- 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 FH by Simon-Broome Diagnostic Criteria or Dutch Lipid Clinic Network Criteria (See Appendix D) 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

V. 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. Non-Hodgkin lymphoma (NHL) with any of the following subtypes:
      a. AIDS-related diffuse large B-cell lymphoma
      b. Primary effusion lymphoma
      c. Lymphoma associated with Castleman’s disease
      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. 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 effusion lymphoma
   3. Lymphoma associated with Castleman’s disease
   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

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.

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

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.

FDA-Approved Indications
1. Adult patients with follicular lymphoma (FL):
   a. Relapsed or refractory, follicular lymphoma as a single agent
   b. 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
   c. 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:
1. Initiate treatment with Rituxan Hycela only after patients have received at least one full dose of a rituximab product by intravenous infusion.
2. Rituxan Hycela is not indicated for the treatment of non-malignant conditions.

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

II. 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. Diffuse large B-cell lymphoma (DLBCL)
   Authorization of 12 months may be granted for treatment of CD20 positive DLBCL in combination with cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP) or other anthracycline-based chemotherapy regimens in previously untreated disease.

B. Chronic lymphocytic leukemia (CLL)
   Authorization of 12 months may be granted for treatment of CLL in combination with fludarabine and cyclophosphamide.
C. Follicular lymphoma (FL)
   Authorization of 12 months may be granted for treatment of CD20 positive FL when used in any of the following settings:
   1. As a single agent for relapsed or refractory disease
   2. In combination with first line chemotherapy in previously untreated disease
   3. As a single agent for maintenance therapy when member has achieved a complete or partial response to rituximab in combination with chemotherapy
   4. As a single agent in non-progressing disease after first-line cyclophosphamide, vincristine, and prednisone (CVP) 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

RITUXAN (rituximab)
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 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 Rituxan 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 patients with previously untreated and previously treated CD20-positive CLL.
3. Granulomatosis with polyangiitis (Wegener’s Granulomatosis) and microscopic polyangiitis (MPA) (Not addressed in this policy – Refer to Rituxan-RA+Other SGM)
4. Moderately to severely active rheumatoid arthritis (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. Castleman’s disease
   g. Acquired immunodeficiency syndrome (AIDS)-related B-cell lymphoma
   h. Hairy cell leukemia
   i. Post-transplant lymphoproliferative disorder (PTLD)
   j. Lymphoblastic lymphoma
6. Relapsed/refractory immune or idiopathic thrombocytopenic purpura (ITP)\textsuperscript{2,6}
7. Autoimmune hemolytic anemia\textsuperscript{2,7}
8. Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma (LPL)\textsuperscript{2,3}
9. Thrombotic thrombocytopenic purpura\textsuperscript{2,4}
10. Myasthenia gravis, refractory\textsuperscript{2}
11. Hodgkin’s lymphoma, nodular lymphocyte-predominant\textsuperscript{2,3}
12. Chronic graft-versus-host disease (GVHD)\textsuperscript{2,9}
13. Central nervous system (CNS) cancers\textsuperscript{3}
   a. Leptomeningeal metastases from lymphomas
   b. Primary CNS lymphoma
14. Acute lymphoblastic leukemia (ALL)\textsuperscript{3}
15. Prevention of Epstein-Barr virus (EBV)-related PTLD in high risk patients\textsuperscript{2,8,10}
16. Immune checkpoint inhibitor-related toxicities\textsuperscript{3}

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

CRITERIA FOR INITIAL APPROVAL

A. Oncologic indications\textsuperscript{1-5}
   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. Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)
      c. Follicular lymphoma
      d. Mantle cell lymphoma
      e. Marginal zone lymphomas (nodal, splenic, gastric/non-gastric MALT)
      f. Burkitt lymphoma
      g. Primary cutaneous B-cell lymphoma
      h. Castleman’s disease
      i. AIDS-related B-cell lymphoma
      j. Hairy cell leukemia
      k. Post-transplant lymphoproliferative disorder (PTLD)
      l. 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. Acute lymphoblastic leukemia (ALL)

B. Hematologic indications\textsuperscript{2,6-10}
   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\textsuperscript{2}
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.

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

III. REFERENCES
SPECIALTY GUIDELINE MANAGEMENT

RITUXAN (rituximab)
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., Xelijanz) 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

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, 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


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.

FDA-Approved Indications
A. 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.

B. 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).

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 newly diagnosed FLT3 mutation-positive AML when Rydapt is/was used in combination with standard cytarabine with daunorubicin or idarubicin induction followed by cytarabine consolidation chemotherapy.

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

PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>BRAND NAME</th>
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**Status:** CVS Caremark Criteria  
**Type:** Initial Prior Authorization  
Ref # 1227-A

**FDA-APPROVED INDICATIONS**
Saxenda 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 comorbid condition (e.g., hypertension, type 2 diabetes mellitus, or dyslipidemia)

**Limitations of Use**
- Saxenda is not indicated for the treatment of type 2 diabetes mellitus.
- Saxenda and Victoza both contain the same active ingredient, liraglutide, and therefore should not be used together. Saxenda should not be used in combination with any other GLP-1 receptor agonist.
- Saxenda has not been studied in patients taking insulin. Saxenda and insulin should not be used together.
- The effects of Saxenda on cardiovascular morbidity and mortality have not been established.
- The safety and effectiveness of Saxenda in combination with other products intended for weight loss, including prescription drugs, over-the-counter drugs, and herbal preparations, have not been established.
- Saxenda has not been studied in patients with a history of pancreatitis.

**COVERAGE CRITERIA**
Saxenda will be covered with prior authorization when the following criteria are met:
- The patient has been receiving the requested drug for at least 16 weeks and the patient lost at least 4 percent of baseline body weight or has continued to maintain their weight loss  
**OR**
- The requested medication 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. Saxenda 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 comorbid condition (e.g., hypertension, type 2 diabetes mellitus, or dyslipidemia). Saxenda is not indicated for the treatment of type 2 diabetes mellitus. Saxenda and Victoza both contain the same active ingredient, liraglutide, and therefore should not be used together. Saxenda should not be used in combination with any other GLP-1 receptor agonist. Saxenda has not been studied in patients taking insulin. Saxenda and insulin should not be used together. The effects of Saxenda on cardiovascular morbidity and mortality have not been established. The safety and effectiveness of Saxenda in combination with other products intended for weight loss, including prescription drugs, over-the-counter drugs, and herbal preparations, have not been established. Saxenda has not been studied in patients with a history of pancreatitis.

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 > 30 kg/m² or ≥ 27 kg/m² if other risk factors are present (e.g., hypertension, diabetes, dyslipidemia, sleep apnea, cardiovascular disease).4-7

Safety and effectiveness of Saxenda have not been established in pediatric patients. Saxenda is not recommended for use in pediatric patients.

The safety and efficacy of Saxenda for chronic weight management in conjunction with reduced caloric intake and increased physical activity were studied in three 56-week, randomized, double-blind, placebo-controlled trials. In all studies, Saxenda was titrated to 3 mg daily during a 4-week period. All patients received instruction for a reduced calorie diet (approximately 500 kcal/day deficit) and exercise counseling (recommended increase in physical activity of minimum 150 mins/week) that began with the first dose of study medication or placebo and continued throughout the trial.

For renewal after 16 weeks of Saxenda therapy, the patient must have lost at least 4% of baseline body weight or have continued to maintain their weight loss. It is recommended that Saxenda therapy be discontinued after 16 weeks if the patient did 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.

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 reevaluated with the patient and lack of long-term data is acknowledged.4-6

REFERENCES

CRITERIA FOR APPROVAL

1. Has the patient completed at least 16 weeks of therapy with the requested drug? [If no, then skip to question 3.]
   - Yes
   - No

2. Did the patient lose at least 4 percent of baseline body weight or has the patient continued to maintain their weight loss?
   - Yes
   - No
[No further questions required.]

3 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 5.]  
Yes No

4 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

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

---

### Guidelines for Approval

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### Mapping Instructions

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|     | 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 use of this drug does not meet the requirements. This is based on the information we have. |
| 5.  | Approve for 4 months. | Deny                                    |
|     | Your plan covers this drug when you will diet and exercise.  
Your use of this drug does not meet the requirement. This is based on the information we have. |
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 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 24 months may be granted for the 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 24 months may be granted for the 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 24 months may be granted for the 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 24 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

All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria, except for the requirement of a serum calcium level (corrected for albumin) greater than or equal to 8.4 mg/dL.
IV. APPENDIX

Corrected calcium = measured total calcium + 0.8(4.0 – serum albumin)

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

- Treatment of patients with acromegaly who have had an inadequate response to surgery and/or for whom surgery is not an option
- 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

sildenafil tablets (generic)
Revatio (sildenafil tablets and oral 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
Sildenafil/Revatio is indicated for the treatment of pulmonary arterial hypertension (WHO Group I) in adults to improve exercise ability and delay clinical worsening.

B. Compendial Use
Raynaud’s phenomenon secondary to systemic sclerosis (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 (1) or criterion (2) below:
   i. Pretreatment right heart catheterization with all of the following results:
      • mPAP ≥ 25 mmHg
      • PCWP ≤ 15 mmHg
      • 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:
      • Post cardiac surgery
      • Chronic heart disease
      • Chronic lung disease associated with prematurity
      • Congenital diaphragmatic hernia

B. Secondary Raynaud’s Phenomenon
Authorization of 12 months may be granted for treatment Raynaud’s phenomenon secondary to systemic sclerosis when the patient has had an inadequate response to one of the following medications:
• Calcium channel blockers
• Angiotensin receptor blockers
• Selective serotonin reuptake inhibitors
• Alpha blockers
• Angiotensin converting enzyme inhibitors
• Topical nitrates
III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with PAH or secondary Raynaud’s phenomenon who are currently receiving sildenafil/Revatio therapy through a paid pharmacy or medical benefit.

IV. APPENDIX

WHO Classification of Pulmonary Hypertension

WHO Group 1. Pulmonary Arterial Hypertension (PAH)
1.1 Idiopathic (IPA)
1.2 Heritable PAH
   1.2.1 Germline mutations in the bone morphogenetic protein receptor type 2 (BMPR2)
   1.2.2 Activin receptor-like kinase type 1 (ALK1), endoglin (with or without hereditary hemorrhagic telangiectasia), Smad 9, caveolin-1 (CAV1), potassium channel super family K member-3 (KCNK3)
   1.2.3 Unknown
1.3 Drug- and toxin-induced
1.4. 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’. Pulmonary veno-occlusive disease (PVOD) and/or pulmonary capillary hemangiomatosis (PCH)
1”. Persistent pulmonary hypertension of the newborn (PPHN)

WHO Group 2. Pulmonary Hypertension Owing to Left Heart Disease
2.1 Systolic dysfunction
2.2 Diastolic dysfunction
2.3 Valvular disease
2.4 Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies

WHO Group 3. Pulmonary Hypertension Owing to Lung Disease and/or Hypoxia
3.1 Chronic obstructive pulmonary disease
3.2 Interstitial lung disease
3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
3.4 Sleep-disordered breathing
3.5 Alveolar hypoventilation disorders
3.6 Chronic exposure to high altitude
3.7 Developmental abnormalities

WHO Group 4. Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

WHO Group 5. Pulmonary Hypertension with Unclear Multifactorial Mechanisms
5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders, splenectomy
5.2 Systemic disorders: sarcoidosis, pulmonary Langerhans cell histiocytosis: lymphangioleiomyomatosis, neurofibromatosis, vasculitis
5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
5.4 Others: tumoral obstruction, fibrosing mediastinitis, chronic renal failure on dialysis, segmental PH

V. 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):

1. Adrenal gland tumors
2. Tumors of the gastrointestinal (GI) tract, lung, and thymus (carcinoid tumors)
3. 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 metastatic or unresectable NETs of the GI tract.

2. Tumors of the thymus (carcinoid tumor)

   Authorization of 24 months may be granted for treatment of metastatic or unresectable NETs of the thymus.

3. Tumors of the lung (carcinoid tumor)

   Authorization of 24 months may be granted for treatment of metastatic or unresectable NETs of the lung.
4. Tumors of the pancreas
   Authorization of 24 months may be granted for treatment of NETs of the pancreas.

5. Tumors of the adrenal gland
   Authorization of 24 months may be granted for treatment of NETs of the adrenal gland.

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

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.

B. Compendial Uses

Neuroendocrine tumors (NETs):

1. Adrenal gland tumors
2. Tumors of the gastrointestinal (GI) tract, lung, and thymus (carcinoid tumors)
3. 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 12 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 12 months may be granted for treatment of metastatic or unresectable NETs of the GI tract.
2. Tumors of the thymus (carcinoid tumor)
   Authorization of 12 months may be granted for treatment of metastatic or unresectable NETs of the thymus.
3. Tumors of the lung (carcinoid tumor)
   Authorization of 12 months may be granted for treatment of metastatic or unresectable NETs of the lung.
4. Tumors of the pancreas
   Authorization of 12 months may be granted for treatment of NETs of the pancreas.
5. Tumors of the adrenal gland
   Authorization of 12 months may be granted for treatment of NETs of the adrenal gland.
III. CONTINUATION OF THERAPY

A. Acromegaly
   Authorization of 12 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

SOMAVERT (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

SOMAVERG (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 12 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 12 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 genotype 1, 2, 3 or 4 chronic hepatitis C virus (HCV) infection as a component of a combination antiviral treatment regimen.

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

II. EXCLUSIONS
Prior treatment failure with an HCV protease inhibitor (eg, telaprevir, simeprevir, boceprevir, paritaprevir) despite adequate dosing and duration of therapy for members prescribed a treatment regimen that includes Olysio.

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 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 and have a fibrosis score ≥F1 or who failed prior treatment with PEG-IFN and RBV.
   2. Genotype 4 infection
      Authorization of up to 12 weeks total may be granted for members who are treatment-naïve and have a fibrosis score ≥F1 or who failed prior treatment with PEG-IFN and RBV.

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 IV) and have a fibrosis score >F1.
   2. Genotype 2 infection
      Authorization of up to 12 weeks total may be granted for members who are treatment-naïve and have a fibrosis score ≥F1 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 and have a fibrosis score ≥F1 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
5. **Recurrent HCV infection post liver transplantation**
   Authorization of up to 24 weeks total may be granted for members with compensated cirrhosis or with decompensated cirrhosis who have recurrent HCV genotype 2 infection post liver transplantation.

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. **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, or D above are met.

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 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. Treatment of newly diagnosed adults with Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in chronic phase
   2. Treatment of adults with chronic, accelerated, or myeloid or lymphoid blast phase Ph+ CML with resistance or intolerance to prior therapy including imatinib
   3. Treatment of adults with Ph+ acute lymphoblastic leukemia (ALL) with resistance or intolerance to prior therapy
   4. Treatment of pediatric patients with Ph+ CML in chronic phase

B. Compendial Uses
   1. 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. Follow-up therapy for CML patients resistant or intolerant to primary treatment with another tyrosine kinase inhibitor (TKI)
   4. Ph+ ALL as a single agent or in combination with chemotherapy or corticosteroids
   5. 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. CRITERIA FOR INITIAL APPROVAL

A. Chronic Myelogenous Leukemia, Chronic Phase (CP-CML)

Authorization of 12 months may be granted for members initiating Sprycel for the treatment of CP-CML when all of the following criteria are met:

1. Diagnosis of CML was confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing.
2. Member meets ANY of the following criteria:
   a. Member is less than or equal to 21 years of age.
   b. Member has a high or intermediate risk score according to the Sokal or Hasford scoring methodology.
   c. Member has a low risk score according to the Sokal or Hasford scoring methodology AND meets EITHER of the following:
      i. Member has experienced resistance to prior therapy with imatinib or an alternate TKI AND results of mutational testing are negative for T315I mutation.
      ii. Member has experienced toxicity or intolerance to prior therapy with imatinib or an alternate TKI.
B. Chronic Myelogenous Leukemia, Accelerated Phase (AP-CML) or Blast Phase (BP-CML)
Authorization of 12 months may be granted for members initiating Sprycel for the treatment of AP-CML or BP-CML when diagnosis was confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing.

C. CML, Post-Hematopoietic Stem Cell Transplant (HSCT)
Authorization of 12 months may be granted for members who are initiating treatment with Sprycel and have received a HSCT for CML when diagnosis was confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing.

D. Ph+ Acute Lymphoblastic Leukemia (ALL)
Authorization of 12 months may be granted for members who are prescribed Sprycel for the treatment of ALL when diagnosis was confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing.

E. Gastrointestinal stromal tumor (GIST)
Authorization of 12 months may be granted for members who are prescribed Sprycel for the treatment of GIST and have experienced disease progression on imatinib, sunitinib, or regorafenib.

III. CONTINUATION OF THERAPY
All members (including new members) requesting authorization for continuation of therapy must meet ALL diagnosis-specific authorization criteria below:

A. Chronic Myelogenous Leukemia (CML)
Authorization of up to 12 months may be granted for members continuing treatment with Sprycel for CML when ALL of the following criteria are met:
1. Diagnosis of CML was confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing.
2. Member meets ANY of the following criteria:
   a. Authorization of up to 12 months for members with chronic phase CML if receiving benefit from Sprycel therapy (i.e., achieved or maintained a cytogenic or molecular response to therapy).
   b. Authorization of 12 months for members with accelerated or blast phase CML.
   c. Authorization of 12 months for members who have received a HSCT for CML (any phase).

B. Ph+ Acute Lymphoblastic Leukemia (ALL)
All members (including new members) requesting authorization for continuation of Sprycel therapy for Ph+ ALL must meet ALL initial authorization criteria.

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

IV. 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

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
2. Active psoriatic arthritis
3. Moderately to severely active Crohn’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 are 12 years of age or older and who have received Stelara, Otezla, or any other biologic DMARD indicated for the treatment of moderate to severe plaque psoriasis in a paid claim through a pharmacy or medical benefit in the previous 120 days of the initial request for Stelara.

2. Authorization of 24 months may be granted for treatment of moderate to severe plaque psoriasis in members 12 years of age and older when all of the following criteria is 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)
1. Authorization of 24 months may be granted for members who are 18 years of age or older and who have received Stelara, Cosentyx or Otezla in a paid claim through a pharmacy or medical benefit in the previous 120 days of the initial request for Stelara.

2. Authorization of 24 months may be granted for treatment of active PsA in members 18 years of age or older when any of the following criteria is met:
   a. Member has had an inadequate response to at least a 3-month trial of at least one TNF inhibitor indicated for PsA (see Appendix B).
b. Member has experienced an intolerance or adverse event to a trial of at least one TNF inhibitor indicated for PsA.

c. All TNF inhibitors indicated for PsA are not appropriate for the member (e.g., due to comorbidities or a history of infections).

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 and who have received Stelara or any other biologic indicated for the treatment of Crohn's disease in a paid claim through a pharmacy or medical benefit in the previous 120 days of the initial request for Stelara.

2. Authorization of 24 months may be granted for members who are 18 years of age or older and who have had an inadequate response, intolerance or contraindication to EITHER of the following:
   a. At least ONE conventional therapy option (see Appendix C)
   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) in a paid claim through a pharmacy or medical benefit in the previous 120 days of the continuation request 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 (male or female)
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)
Appendix B: TNF Inhibitors Indicated for Psoriatic Arthritis
1. Cimzia® (certolizumab pegol)
2. Enbrel® (etanercept)
3. Humira® (adalimumab)
4. Remicade® (infliximab)
5. Simponi® (golimumab)

Appendix C: Examples of Conventional Therapy Options for CD
1. Mild to moderate disease – induction of remission:
   a. Oral budesonide, oral mesalamine
   b. Alternatives: metronidazole, ciprofloxacin, rifaximin
2. Mild to moderate disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternatives: oral budesonide, methotrexate intramuscularly (IM)
3. Moderate to severe disease – induction of remission:
   a. Prednisone, methylprednisolone intravenously (IV)
   b. Alternatives: methotrexate IM
4. Moderate to severe disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: methotrexate IM
5. Perianal and fistulizing disease – induction of remission:
   a. Metronidazole ± ciprofloxacin
6. Perianal and fistulizing disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: methotrexate IM

VI. REFERENCES
PRIOR AUTHORIZATION CRITERIA

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FDA-APPROVED INDICATIONS
Attention-Deficit/Hyperactivity Disorder (ADHD)
Strattera is indicated for the treatment of Attention-Deficit/Hyperactivity Disorder (ADHD). The efficacy of Strattera was established in seven clinical trials in outpatients with ADHD: four 6 to 9-week trials in pediatric patients (ages 6 to 18), two 10-week trials in adults, and one maintenance trial in pediatrics (ages 6 to 15).

Diagnostic Considerations
A diagnosis of ADHD (DSM-IV) implies the presence of hyperactive-impulsive or inattentive symptoms that cause impairment and that were present before age 7 years. The symptoms must be persistent, must be more severe than is typically observed in individuals at a comparable level of development, must cause clinically significant impairment, e.g., in social, academic, or occupational functioning, and must be present in 2 or more settings, e.g., school (or work) and at home. The symptoms must not be better accounted for by another mental disorder.

The specific etiology of ADHD is unknown, and there is no single diagnostic test. Adequate diagnosis requires the use not only of medical but also of special psychological, educational, and social resources. Learning may or may not be impaired. The diagnosis must be based upon a complete history and evaluation of the patient and not solely on the presence of the required number of DSM-IV characteristics.

For the Inattentive Type, at least 6 of the following symptoms must have persisted for at least 6 months: lack of attention to details/careless mistakes, lack of sustained attention, poor listener, failure to follow through on tasks, poor organization, avoids tasks requiring sustained mental effort, loses things, easily distracted, forgetful. For the Hyperactive-Impulsive Type, at least 6 of the following symptoms must have persisted for at least 6 months: fidgeting/squirming, leaving seat, inappropriate running/climbing, difficulty with quiet activities, “on the go,” excessive talking, blurtling answers, can’t wait turn, intrusive. For a Combined Type diagnosis, both inattentive and hyperactive-impulsive criteria must be met.

Need for Comprehensive Treatment Program
Strattera is indicated as an integral part of a total treatment program for ADHD that may include other measures (psychological, educational, social) for patients with this syndrome. Drug treatment may not be indicated for all patients with this syndrome. Drug treatment is not intended for use in the patient who exhibits symptoms secondary to environmental factors and/or other primary psychiatric disorders, including psychosis. Appropriate educational placement is essential in children and adolescents with this diagnosis and psychosocial intervention is often helpful. When remedial measures alone are insufficient, the decision to prescribe drug treatment medication will depend upon the physician’s assessment of the chronicity and severity of the patient’s symptoms.

COVERAGE CRITERIA
Strattera will be covered with prior authorization when the following criteria are met:

- The patient has a diagnosis of Attention-Deficit Hyperactivity Disorder (ADHD) or Attention Deficit Disorder (ADD) AND
- The patient will be monitored closely for suicidal thinking or behavior, clinical worsening, and unusual changes in behavior
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. Strattera is indicated for the treatment of Attention-Deficit / Hyperactivity Disorder (ADHD).

The patient should be monitored for suicidality (suicidal thinking and behavior), clinical worsening, and unusual changes in behavior.

The American Academy of Pediatrics Clinical Practice Guideline states that stimulant medications are highly effective for most children in reducing core symptoms of ADHD; however, atomoxetine has also demonstrated efficacy in reducing core symptoms. Additionally, when there is a concern about the potential for drug misuse and diversion, atomoxetine or stimulant medications with less abuse potential may be considered.4

REFERENCES
CRITERIA FOR APPROVAL

1. Does the patient have a diagnosis of Attention-Deficit Hyperactivity Disorder (ADHD) or Attention Deficit Disorder (ADD)?
   - Yes
   - No

2. Will the patient be monitored closely for suicidal thinking or behavior, clinical worsening, and unusual changes in behavior?
   - Yes
   - No

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PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

STRATTERA
(atomoxetine HCl)

Status:  CVS Caremark Criteria
Type:  Initial Prior Authorization
Ref # 876-A
Ref # MDC-2 215-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
Strattera is indicated for the treatment of Attention-Deficit/Hyperactivity Disorder (ADHD).
The efficacy of Strattera was established in seven clinical trials in outpatients with ADHD: four 6 to 9-week trials in pediatric patients (ages 6 to 18), two 10-week trials in adults, and one maintenance trial in pediatrics (ages 6 to 15).

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:
- The patient has a diagnosis of Attention-Deficit Hyperactivity Disorder (ADHD) or Attention Deficit Disorder (ADD)
AND
- The patient will be monitored closely for suicidal thinking or behavior, clinical worsening, and unusual changes in behavior.

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. Strattera is indicated for the treatment of Attention-Deficit / Hyperactivity Disorder (ADHD).

The patient should be monitored for suicidality (suicidal thinking and behavior), clinical worsening, and unusual changes in behavior.

The American Academy of Pediatrics Clinical Practice Guideline states that stimulant medications are highly effective for most children in reducing core symptoms of ADHD; however, atomoxetine has also demonstrated efficacy in reducing core symptoms. Additionally, when there is a concern about the potential for drug misuse and diversion, atomoxetine or stimulant medications with less abuse potential may be considered.4

REFERENCES
CRITERIA FOR APPROVAL

1. Does the patient have a diagnosis of Attention-Deficit Hyperactivity Disorder (ADHD) or Attention Deficit Disorder (ADD)?
   - Yes
   - No

2. Will the patient be monitored closely for suicidal thinking or behavior, clinical worsening, and unusual changes in behavior?
   - Yes
   - No

Mapping Instructions (876-A)

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</tr>
<tr>
<td>2. Approve, 36 months</td>
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</table>

DENIAL REASONS – DO NOT USE FOR MEDICARE PART D

- Your plan covers this drug when you meet these conditions:
  - You have Attention-Deficit Hyperactivity Disorder (ADHD) or Attention Deficit Disorder (ADD)
  - Your use of this drug does not meet the requirements. This is based on the information we have.

Guidelines for Approval (MDC-2 215-A)

<table>
<thead>
<tr>
<th>Duration of Approval</th>
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<tr>
<td>Yes to question(s)</td>
<td>No to question(s)</td>
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<tr>
<td>1</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td></td>
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Mapping Instructions (MDC-2 215-A)

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<tbody>
<tr>
<td>3. Go to 2</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

- Your plan covers this drug when you meet these conditions:
  - You have Attention-Deficit Hyperactivity Disorder (ADHD) or Attention Deficit Disorder (ADD)
  - Your use of this drug does not meet the requirements. This is based on the information we have.
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. Advanced renal cell carcinoma (RCC)
   2. Adult patients at high risk of recurrent RCC following nephrectomy
   3. Gastrointestinal stromal tumor (GIST) after disease progression on or intolerance to imatinib
   4. Progressive, well-differentiated pancreatic neuroendocrine tumors (PNETs) 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
      b. Solitary fibrous tumor
      c. Hemangiopericytoma
   3. Thymic carcinoma
   4. Medullary, papillary, Hürthle cell, or follicular thyroid carcinoma
   5. Chordoma

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 RCC when either of the following criteria is met:
   1. Disease is relapsed, metastatic or unresectable
   2. Member is at high risk of recurrent RCC following nephrectomy

B. Soft Tissue Sarcoma
   Authorization of 12 months may be granted for treatment of the following subtypes of STS: gastrointestinal stromal tumor, angiosarcoma, solitary fibrous tumor, and hemangiopericytoma.

C. Pancreatic Neuroendocrine Tumor
   Authorization of 12 months may be granted for treatment of pancreatic neuroendocrine tumors.

D. Thymic Carcinoma
   Authorization of 12 months may be granted for treatment of thymic carcinoma.
E. Thyroid Carcinoma²,⁸
Authorization of 12 months may be granted for treatment of thyroid carcinoma with any of the following histologies: papillary, Hurthle cell, follicular, or medullary.

F. Chordoma²
Authorization of 12 months may be granted for treatment of chordoma.

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
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 Use:
   1. Symptomatic low-risk myelofibrosis

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 with microscopic or gross nodal involvement.

B. Myelofibrosis

   Authorization of 12 months may be granted for the treatment of 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

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 a combination of tezacaftor and ivacaftor, indicated for the treatment of patients with cystic fibrosis (CF) aged 12 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 12 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

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
2. Bone cancer – chordoma
3. Renal cell carcinoma

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

II. 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 has a known sensitizing EGFR mutation.

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 RCC.
D. Chordoma

Authorization of 12 months may be granted for treatment of chordoma.

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

III. CONTINUATION OF THERAPY

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

IV. REFERENCE

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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:
   a. Anaplastic gliomas
   b. Intracranial and spinal ependymoma
   c. Supratentorial astrocytoma/oligodendroglioma
   d. Medulloblastoma/supratentorial primitive neuroectodermal tumors (PNET)
   e. CNS metastases
   f. Primary CNS lymphoma

2. Ewing's sarcoma

3. Neuroendocrine tumors of pancreas, gastrointestinal tract, lung, and thymus

4. Pheochromocytoma/paraganglioma

5. Melanoma

6. Mycosis fungoides/Sézary syndrome

7. Dermatofibrosarcoma protuberans

8. Small cell lung cancer

9. Soft tissue sarcoma:
   a. Angiosarcoma
   b. Retroperitoneal/intra-abdominal
   c. Rhabdomyosarcoma
   d. Solitary fibrous tumor and hemangiopericytoma
   e. Of the extremity/trunk, head/neck

10. Uterine sarcoma

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 any of the following CNS cancers:
1. Glioblastoma
2. Anaplastic glioma
3. Intracranial and spinal ependymoma
4. Supratentorial astrocytoma/oligodendroglioma
5. Medulloblastoma and supratentorial primitive neuroectodermal tumors (PNET)
6. Brain metastases
7. Primary CNS lymphoma (PCNSL)

B. Ewing's sarcoma
Authorization of 12 months may be granted for treatment of Ewing's 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. Pheochromocytoma/paraganglioma
Authorization of 12 months may be granted for treatment of pheochromocytoma or paraganglioma.

E. Melanoma
Authorization of 12 months may be granted for treatment of metastatic or unresectable melanoma.

F. Mycosis fungoides/Sezary syndrome
Authorization of 12 months may be granted for treatment of mycosis fungoides/Sezary syndrome.

G. Dermatofibrosarcoma protuberans (DFSP)
Authorization of 12 months may be granted for treatment of metastatic disease.

H. Small cell lung cancer (SCLC)
Authorization of 12 months may be granted for treatment of SCLC.

I. Soft tissue sarcoma (STS)
Authorization of 12 months may be granted for treatment of any of the following STS:
1. Angiosarcoma
2. Retroperitoneal/intra-abdominal STS
3. Rhabdomyosarcoma
4. Solitary fibrous tumor and hemangiopericytoma
5. STS of the extremity/trunk, head/neck

J. Uterine sarcoma
Authorization of 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. REFERENCES

# PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>TESTOSTERONE PRODUCTS – INJECTABLE</th>
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<tbody>
<tr>
<td>BRAND NAME (generic)</td>
<td>DELATESTRYL (testosterone enanthate injection)</td>
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</table>

**Status:** CVS Caremark Criteria  
**Type:** Initial Prior Authorization  
**Ref #** 1368-A

## FDA-APPROVED INDICATIONS

### 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 orchietomy.

**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 counteracting estrogen activity are adrenalec-tomy, 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.

## Compendial Uses
Gender Dysphoria in Female-to-Male transgender patients

## COVERAGE CRITERIA
- Delatestryl (testosterone enanthate injection) will be covered with prior authorization when the following criteria are met:
  - The requested drug 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
  - The requested drug 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

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OR
  o  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 male 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 male lab reference values
OR
  o  The requested drug is being prescribed for delayed puberty
OR
  o  The requested drug is being prescribed for female-to-male gender reassignment in a patient who is 14 years of age or older and able to make an informed, mature decision to engage in therapy

RATIONAL
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 orchiectomy), hypogonadotropic hypogonadism (gonadotropin or LHRH deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation), and delayed puberty. Safety and efficacy of Delatestryl in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.1-3

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 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.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.

For continuation of therapy, one low testosterone level is required before the patient started testosterone therapy.

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

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 is arbitrary, 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. Therefore, individuals aged 14
years and older who are able to make an informed, mature decision to engage in therapy will be approved.

For female-to-male (FtM) transgender 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 FtM 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
FtM 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 FtM patient.

REFERENCES
2. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.;
Practice for the Evaluation and Treatment of Hypogonadism in Adult Male Patients – 2002 update. Endocrine Practice
An Endocrine Society Clinical Practice Guideline. Journal of Clinical Endocrinology & Metabolism 2010 95(6):2536-
2559.
Sep;94(9):3132-54.
Nonconforming People. World Professional Association for Transgender Health. Last Updated 2012. Available at:
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<tr>
<th>CRITERIA FOR APPROVAL</th>
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</tr>
</thead>
<tbody>
<tr>
<td>1. Is the requested drug being prescribed for inoperable metastatic breast cancer in</td>
<td></td>
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<tr>
<td>a patient who is 1 to 5 years postmenopausal AND has the patient had an incomplete response to</td>
<td></td>
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<tr>
<td>other therapy for metastatic breast cancer? [If yes, then no further questions.]</td>
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<td></td>
</tr>
<tr>
<td>2. Is the requested drug being prescribed for a pre-menopausal patient with breast cancer who has benefited from oophorectomy and is considered to have a hormone-responsive tumor? [If yes, then no further questions.]</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>3. 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 7.]</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>4. Is this request for a continuation of testosterone therapy? [If no, then skip to question 6.]</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>5. Before the patient started testosterone therapy, did the patient have a confirmed low testosterone level according to current practice guidelines or your standard male lab reference values? [No further questions.]</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>6. Does the patient have at least two confirmed low testosterone levels according to current practice guidelines or your standard male lab reference values? [No further questions.]</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>7. Is the requested drug being prescribed for delayed puberty? [If yes, then no further questions.]</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>8. Is the requested drug being prescribed for female-to-male gender reassignment in a patient who is 14 years of age or older and able to make an informed, mature decision to engage in therapy?</td>
<td>Yes</td>
<td>No</td>
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</table>

| Mapping Instructions                                                                 |
|--------------------------------------------------------------------------------------|-----|-----|
| **Yes**                                                                              | No  |     |
| 1. Approve, 12 Months                                                                  | Go to 2 |
| 2. Approve, 12 Months                                                                  | Go to 3 |
| 3. Go to 4                                                                             | Go to 7 |
| 4. Go to 5                                                                             | Go to 6 |
| 5. Approve, 12 months                                                                  | Deny |

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

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 use of this drug does not meet the requirements. This is based on the information we have.
<table>
<thead>
<tr>
<th></th>
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<th>Deny</th>
<th></th>
</tr>
</thead>
</table>
| 6 |                   | 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 use of this drug does not meet the requirements. This is based on the information we have. |
| 7 | Approve, 12 Months | Go to 8 | |
| 8 | Approve, 12 Months | Deny | Your plan covers this drug when you meet one of these conditions:  
- You have delayed puberty  
- You have primary or hypogonadotropic hypogonadism  
- You are a postmenopausal patient with metastatic breast cancer, surgery is not possible, and other drugs for your cancer did not work for you  
- You are a premenopausal patient with breast cancer, have a hormone-responsive tumor, and had your ovaries removed  
Your use of this drug does not meet the requirement. This is based on the information we have.  
Your plan also covers this drug when you meet all of these conditions:  
- You are using it to change your gender from female to male  
- You are 14 years of age or older  
- You are able to make an informed, mature decision to use this drug  
Your use of this drug does not meet the requirements. This is based on the information we have. |
PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>TESTOSTERONE PRODUCTS - INJECTABLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRAND NAME (generic)</td>
<td>DEPO-TESTOSTERONE (testosterone cypionate injection)</td>
</tr>
</tbody>
</table>

Status: CVS Caremark Criteria
Type: Initial Prior Authorization
MDC-2
Ref # 976-A

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 Female-to-Male transgender patients

COVERAGE CRITERIA
- Depo-Testosterone (testosterone cypionate injection) 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 male 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 male lab reference values

  OR
  - The requested drug is being prescribed for female-to-male gender reassignment in a patient who is 14 years of age or older and able to make an informed, mature decision to engage in 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. 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). 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. 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 female-to-male transgender 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 is arbitrary, 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.\(^6\) Therefore, individuals aged 14 years and older who are able to make an informed, mature decision to engage in therapy will be approved.

For female-to-male (FtM) transgender 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 FtM 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 FtM patients is intramuscular injection of testosterone esters (cypionate or enanthate).\(^7\)

**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 male 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 male lab reference values?  
   [No further questions.]  
   Yes No

5. Is the requested drug being prescribed for female-to-male gender reassignment in a patient who is 14 years of age or older and able to make an informed, mature decision to engage in therapy?  
   Yes No

Mapping Instructions

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Go to 2</td>
<td>Go to 5</td>
</tr>
<tr>
<td>Go to 3</td>
<td>Go to 4</td>
</tr>
<tr>
<td>Approve, 12 months</td>
<td>Deny</td>
</tr>
</tbody>
</table>

DENIAL REASONS – DO NOT USE FOR MEDICARE PART D

Your plan covers this drug when you meet all of the following conditions:
- You have primary or hypogonadotropic hypogonadism
- Before starting testosterone therapy, you had a test that showed low testosterone levels
Your use of this drug does not meet the requirements. This is based on the information we have.

Your plan covers this drug when you meet all of the following conditions:

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  
| 12 months |  | - You have primary or hypogonadotropic hypogonadism  
- You have had 2 tests that showed low testosterone levels  
Your use of this drug does not meet the requirements. This is based on the information we have. |
|  | 5. Approve, 12 months | Deny | Your plan covers this drug when you have primary or hypogonadotropic hypogonadism. Your use of this drug does not meet the requirement. This is based on the information we have.  
Your plan also covers this drug when you meet all of these conditions:  
- You are using it to change your gender from female to male  
- You are 14 years of age or older  
- You are able to make an informed, mature decision to use this drug  
Your use of this drug does not meet the requirements. This is based on the information we have. |
# Prior Authorization Criteria

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Testosterone Products – Oral</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Brand Name</strong> (Generic)</td>
<td></td>
</tr>
<tr>
<td>Android</td>
<td>(Methyltestosterone, oral capsule)</td>
</tr>
<tr>
<td>Testred</td>
<td>(Methyltestosterone, oral capsule)</td>
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<tr>
<td>Methitest</td>
<td>(Methyltestosterone, oral tablet)</td>
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<tr>
<td>Androxy</td>
<td>(Fluoxymesterone, oral tablet)</td>
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</table>

**Status:** CVS Caremark Criteria  
**Type:** Initial Prior Authorization  
Ref # 878-A

## 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, ororchiectomy.

**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

- Oral testosterone products will be covered with prior authorization when the following criteria are met:
  - The patient has tried and failed or is unable to tolerate one non-oral form of testosterone supplementation
  - The requested drug 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
  - The requested drug 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
  - OR
  - 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 male 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 male lab reference values
  - 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 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

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 countereacting estrogen activity are adrenalectomy, hypophysectomy, and/or anti-estrogen therapy.1-6 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.1-6

Orally administered testosterone is quickly metabolized by the liver and cannot achieve sufficient blood levels over time to be useful. The orally administered alkylated androgen preparations currently available are generally not recommended as first line therapy because of poor androgen effects, adverse lipid changes, and hepatic side effects such as hemorrhagic liver cysts, cholestasis, and hepatocellular adenoma.7 The patient must try and fail or be unable to tolerate one non-oral form of testosterone before oral androgens will be approved.

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. For continuation of therapy, one low testosterone level is required before the patient started testosterone therapy.

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**


**CRITERIA FOR APPROVAL**

1. Has the patient tried and failed or is the patient unable to tolerate one non-oral form of testosterone supplementation? 
   - Yes
   - No

2. Is the requested drug 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? [If yes, then no further questions.]
   - Yes
   - No

3. Is the requested drug being prescribed for a pre-menopausal patient with breast cancer who has benefited from oophorectomy and is considered to have a hormone-responsive tumor? [If yes, then no further questions.]
   - Yes
   - No

4. 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 8.]
   - Yes
   - No
5. **Is this request for a continuation of testosterone therapy?**
   
   [If no, then skip to question 7.]

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<tr>
<th>Yes</th>
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<tbody>
<tr>
<td>5.</td>
<td>2.</td>
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</table>

   | 6.  | 7.  | 8.  |

   | Before the patient started testosterone therapy, did the patient have a confirmed low testosterone level according to current practice guidelines or your standard male lab reference values? |
   | [No further questions.] |

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
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<tbody>
<tr>
<td>6.</td>
<td>7.</td>
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</tbody>
</table>

   | Does the patient have at least two confirmed low testosterone levels according to current practice guidelines or your standard male lab reference values? |
   | [No further questions.] |

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
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<tbody>
<tr>
<td>7.</td>
<td>8.</td>
</tr>
</tbody>
</table>

   | Is requested the drug being prescribed for delayed puberty? |

<table>
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<th>Yes</th>
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</tr>
</thead>
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<tr>
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PRIOR AUTHORIZATION CRITERIA

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<th>DRUG CLASS</th>
<th>TESTOSTERONE PRODUCTS</th>
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<td>BRAND NAME</td>
<td>(generic)</td>
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<td></td>
<td>TESTOPEL</td>
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<td>(testosterone propionate implant pellets)</td>
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</tbody>
</table>

Status: CVS Caremark Criteria
Type: Initial Prior Authorization
Ref # 1369-A

FDA-APPROVED INDICATIONS

Males
Androgens are 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 testes syndrome; or orchiectomy.
Hypogonadotrophic hypogonadism (congenital or acquired) - gonadotropic LHRH deficiency, or pituitary- hypothalamic injury from tumors, trauma or radiation.
If the above conditions occur prior to puberty, androgen replacement therapy will be needed during the adolescent years for development of secondary sex 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 Testopel (testosterone pellets) 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 taken every 6 months to assess the effect of treatment on epiphyseal centers.

Compendial Uses
Gender Dysphoria in Female-to-Male transgender patients

COVERAGE CRITERIA

- Testopel (testosterone propionate implant pellets) 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 male 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 male lab reference values OR
  - The requested drug is being prescribed for delayed puberty

OR
The requested drug is being prescribed for female-to-male gender reassignment in a patient who is 14 years of age or older and able to make an informed, mature decision to engage in 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. Testopel 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 orchiectomy), or hypogonadotropic hypogonadism (gonadotropin LHRH deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation). Safety and efficacy of Testopel (testosterone pellets) 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. For continuation of therapy, one low testosterone level is required before the patient started testosterone therapy.

Testopel 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

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 is arbitrary, 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.6 Therefore, individuals aged 14 years and older who are able to make an informed, mature decision to engage in therapy will be approved.

For female-to-male (FtM) transgender 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 FtM 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 FtM patients is intramuscular injection of testosterone esters (cypionate or enanthate).7 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.8 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 FtM patient.7

REFERENCES
### 1. CRITERIA FOR APPROVAL

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<tr>
<th></th>
<th>Question</th>
<th>Yes</th>
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</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Is the requested drug being prescribed for primary or hypogonadotropic hypogonadism?</td>
<td>Yes</td>
<td>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>
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<td>[If no, then skip to question 5.]</td>
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<td>Is this request for a continuation of testosterone therapy?</td>
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<td>[If no, then skip to question 4.]</td>
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<td>Before the patient started testosterone therapy, did the patient have a confirmed low testosterone level according to current practice guidelines or your standard male lab reference values?</td>
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</tr>
<tr>
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<td>Does the patient have at least two confirmed low testosterone levels according to current practice guidelines or your standard male lab reference values?</td>
<td>Yes</td>
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<td></td>
<td>[No further questions.]</td>
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<td>Is the requested drug being prescribed for delayed puberty?</td>
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<td>No</td>
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<tr>
<td></td>
<td>[If yes, then no further questions.]</td>
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<tr>
<td>6</td>
<td>Is the requested drug being prescribed for female-to-male gender reassignment in a patient who is 14 years of age or older and able to make an informed, mature decision to engage in therapy?</td>
<td>Yes</td>
<td>No</td>
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<td>Yes</td>
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<td>Your plan covers this drug when you meet all of these conditions:</td>
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<td></td>
<td>- You have primary or hypogonadotropic hypogonadism</td>
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<td>- Before starting testosterone therapy, you had a test that showed low testosterone levels</td>
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<td>4. Approve, 12 Months</td>
<td>Deny</td>
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<td></td>
<td>- You have delayed puberty</td>
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<td>Your plan also covers this drug when you meet all of these conditions:</td>
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<td></td>
<td>- You are using it to change your gender from female to male</td>
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</table>
## PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>TESTOSTERONE PRODUCTS – TOPICAL/BUCCAL/NASAL (BRAND AND GENERIC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRAND NAME (generic)</td>
<td>ANDRODERM (testosterone transdermal patch)</td>
</tr>
<tr>
<td></td>
<td>ANDROGEL (testosterone topical gel)</td>
</tr>
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<td>VOGELXO (testosterone topical gel)</td>
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**Status:** CVS Caremark Criteria  
**Type:** Initial Prior Authorization

**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.

COVERAGE CRITERIA
- Testosterone products 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 male 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 male 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.

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 limits 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 limits 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. For continuation of therapy, one low testosterone level is required before the patient started testosterone therapy.
REFERENCES
10. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; 
    Practice for the Evaluation and Treatment of Hypogonadism in Adult Male Patients – 2002 update. Endocrine Practice 
    An Endocrine Society Clinical Practice Guideline. Journal of Clinical Endocrinology & Metabolism 2010 95(6):2536-
    2559. Hembree WC, Cohen-Kettenis P, Delemarre-van de Waal HA, et al; Endocrine Society. Endocrine treatment of 

Written by: UM Development (AH)
Date: 07/2003
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 
10/2012; (DNC) 11/2012; (LCB) 11/2013; (SES) 11/2014; (KRU) 02/2015; (LCB) 11/2015; (MC) 12/2016; (DNC) 02/2017 
02/2017

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 no further questions.]

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 male 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 male lab reference values?
   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>
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<tbody>
<tr>
<td>1. Go to 2</td>
<td>Deny</td>
<td>Your plan covers this drug when you have primary or hypogonadotropic hypogonadism. Your use of this drug does not meet the requirement. This is based on the information we have.</td>
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<tr>
<td>2. Go to 3</td>
<td>Go to 4</td>
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| 3. Approve, 12 months | Deny | 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 use of this drug does not meet the requirements. This is based on the information we have. |
| 4. Approve, 12 months | Deny | 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  
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**PRIOR AUTHORIZATION CRITERIA**

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**Ref # 1370-A**

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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 Female-to-Male transgender patients

COVERAGE CRITERIA
- Testosterone products 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 male 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 male lab reference values
- The requested drug is being prescribed for female-to-male gender reassignment in a patient who is 14 years of age or older and able to make an informed, mature decision to engage in 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). 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. 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. For continuation of therapy, one low testosterone level is required before the patient started testosterone therapy.
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 puberty 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 is arbitrary, 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.\(^{14}\) Therefore, individuals aged 14 years and older who are able to make an informed, mature decision to engage in therapy will be approved.

For female-to-male (FTM) transgender 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).\(^{14}\) The agent primarily used for endocrine treatment of FTM 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 FTM patients is intramuscular injection of testosterone esters (cypionate or enanthate).\(^{15}\) 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.\(^{16}\) 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 lower-normal ranges of testosterone levels in hypogonadal men, which may translate to a lessened change in physical appearance and virilization in the FTM patient.\(^{15}\)

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 male 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 male lab reference values?  
   [No further questions.]  
   Yes  No

5. Is the requested drug being prescribed for female-to-male gender reassignment in a patient who is 14 years of age or older and able to make an informed, mature decision to engage in therapy?  
   Yes  No

Mapping Instructions

<table>
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<tr>
<th>Yes</th>
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<tbody>
<tr>
<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>
<tr>
<td>5. Approve, 12 months</td>
<td>Deny</td>
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DENIAL REASONS – DO NOT USE FOR MEDICARE PART D

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 use of this drug does not meet the requirements. This is based on the information we have.

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 use of this drug does not meet the requirements. This is based on the information we have.

Your plan covers this drug when you meet all of these conditions:  
- You have primary or hypogonadotropic hypogonadism.  
Your plan also covers this drug when you meet all of these conditions:
<p>| | |</p>
<table>
<thead>
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</table>
| - You are using it to change your gender from female to male  
- You are 14 years of age or older  
- You are able to make an informed, mature decision to use this drug  
Your use of this drug does not meet the requirements. This is based on the information we have. |   |
SPECIALTY GUIDELINE MANAGEMENT

XENAZINE (tetrabenazine)
Tetrabenazine (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
   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

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. Systemic light chain amyloidosis
   3. Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma
   4. Multicentric Castleman’s disease
   5. Recurrent aphthous stomatitis
   6. Recurrent HIV-associated aphthous ulcers
   7. Cachexia in patients with cancer or HIV-associated wasting syndrome
   8. Diarrhea in patients with HIV infection
   9. Kaposi’s sarcoma in HIV-infected patients
   10. Behcet’s syndrome
   11. Chronic graft-versus-host disease
   12. 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. Behcet’s Syndrome
   Authorization of 12 months may be granted for treatment of Behcet’s syndrome.

D. Myelofibrosis-related anemia
   Authorization of 12 months may be granted for treatment of myelofibrosis-related anemia.
E. **Systemic Light Chain Amyloidosis**
   Authorization of 12 months may be granted for treatment of systemic light chain amyloidosis.

F. **Erythema Nodosum Leprosum**
   Authorization of 12 months may be granted for treatment of erythema nodosum leprosum.

G. **Crohn's Disease**
   Authorization of 12 months may be granted for treatment of Crohn's disease.

H. **Kaposi's Sarcoma**
   Authorization of 12 months may be granted for treatment of Kaposi's sarcoma in HIV-infected patients.

I. **Chronic Graft-versus-Host Disease**
   Authorization of 12 months may be granted for treatment of chronic graft-versus-host disease.

J. **Waldenström’s Macroglobulinemia/Lymphoplasmacytic Leukemia**
   Authorization of 12 months may be granted for treatment of Waldenström’s macroglobulinemia/lymphoplasmacytic leukemia.

K. **Multicentric Castleman’s Disease**
   Authorization of 12 months may be granted for treatment of multicentric Castleman’s disease.

L. **Recurrent Aphthous Stomatitis**
   Authorization of 12 months may be granted for treatment of recurrent aphthous stomatitis.

M. **Cachexia**
   Authorization of 12 months may be granted for treatment of cachexia caused by cancer or HIV-infection.

N. **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

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 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 12 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

TRACLEER (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

Pulmonary Arterial Hypertension (PAH)

Tracleer is indicated for the treatment of PAH (WHO Group 1):
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.

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:
      • mPAP ≥ 25 mmHg
      • PCWP ≤ 15 mmHg
      • 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:
      • Post cardiac surgery
      • Chronic heart disease
      • Chronic lung disease associated with prematurity
      • Congenital diaphragmatic hernia

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with PAH who are currently receiving Tracleer therapy through a paid pharmacy or medical benefit.

IV. APPENDIX

WHO Classification of Pulmonary Hypertension

WHO Group 1. Pulmonary Arterial Hypertension (PAH)
1.1 Idiopathic (IPAH)
1.2 Heritable PAH
   1.2.1 Germline mutations in the bone morphogenetic protein receptor type 2 (BMPR2)
   1.2.2 Activin receptor-like kinase type 1 (ALK1), endoglin (with or without hereditary hemorrhagic telangiectasia), Smad 9, caveolin-1 (CAV1), potassium channel super family K member-3 (KCNK3)
   1.2.3 Unknown
1.3 Drug- and toxin-induced
1.4. 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’. Pulmonary veno-occlusive disease (PVOD) and/or pulmonary capillary hemangiomatosis (PCH)
1”. Persistent pulmonary hypertension of the newborn (PPHN)

WHO Group 2. Pulmonary Hypertension Owing to Left Heart Disease
2.1 Systolic dysfunction
2.2 Diastolic dysfunction
2.3 Valvular disease
2.4 Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies

WHO Group 3. Pulmonary Hypertension Owing to Lung Disease and/or Hypoxia
3.1 Chronic obstructive pulmonary disease
3.2 Interstitial lung disease
3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
3.4 Sleep-disordered breathing
3.5 Alveolar hypoventilation disorders
3.6 Chronic exposure to high altitude
3.7 Developmental abnormalities

WHO Group 4. Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

WHO Group 5. Pulmonary Hypertension with Unclear Multifactorial Mechanisms
5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders, splenectomy
5.2 Systemic disorders: sarcoidosis, pulmonary Langerhans cell histiocytosis: lymphangioleiomyomatosis, neurofibromatosis, vasculitis
5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
5.4 Others: tumoral obstruction, fibrosing mediastinitis, chronic renal failure on dialysis, segmental PH

V. 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
   1. Palliative treatment of advanced prostate cancer

B. Compendial Uses
   1. Prostate cancer
   2. Gender dysphoria (also known as gender non-conforming or transgender persons)

   \textit{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


# PRIOR AUTHORIZATION CRITERIA

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>RETINOIDS (TOPICAL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRAND NAME</td>
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</tr>
<tr>
<td>(generic)</td>
<td>(tretinoin)</td>
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<tr>
<td></td>
<td>AVITA (ALL TOPICAL)</td>
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<tr>
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<td>(tretinoin)</td>
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<td>RETIN-A (ALL TOPICAL)</td>
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<td>(tretinoin)</td>
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<td>RETIN-A MICRO (ALL TOPICAL)</td>
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<td>(tretinoin gel, microsphere)</td>
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<td>TRETIN-X (ALL TOPICAL)</td>
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<td></td>
<td>(tretinoin)</td>
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<td></td>
<td>VELTIN (ALL TOPICAL)</td>
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<td>(clindamycin/tretinoin gel)</td>
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<td></td>
<td>ZIANA (ALL TOPICAL)</td>
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<td>(clindamycin/tretinoin gel)</td>
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**Status:** CVS Caremark Criteria  
**Type:** Initial Prior Authorization  
**Ref #** 355-A

## FDA-APPROVED INDICATIONS

Atralin, Avita, Retin-A, Retin-A Micro, Tretin-X gel and Tretin-X cream 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.

### Compendial Use

Keratosis follicularis (Darier’s disease, Darier-White disease)\(^{12,15,16}\)

## COVERAGE CRITERIA

Topical Tretinoins 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 guidelines state that topical therapy is a standard of care in acne treatment. 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.\textsuperscript{13, 14}

For 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 have been shown to be effective in reducing the localized symptoms of this disease.\textsuperscript{12,15,16}

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.\textsuperscript{4-5} Since the treatment of these indications is considered cosmetic, these products are not included in the criteria for coverage.

REFERENCES
### CRITERIA FOR APPROVAL

1. Does the patient have the diagnosis of acne vulgaris or keratosis follicularis (Darier’s disease, Darier-White disease)?

<table>
<thead>
<tr>
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#### Mapping Instructions

<table>
<thead>
<tr>
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<th>No</th>
<th>Map: 36 Months Deny</th>
</tr>
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**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**

Your plan covers this drug when you meet one of these conditions:
- You have acne vulgaris
- You have keratosis follicularis (Darier’s disease, Darier-White disease)

Your use of this drug does not meet the requirements. This is based on the information we have.
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 estrogen 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)

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 (eg, 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.

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

TYMLOS™ (abaloparatide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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. CRITERIA FOR APPROVAL

Osteoporosis in Postmenopausal women

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, OR
2. Member has a pre-treatment T-score of ≤ -2.5 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, or increased fall risk), OR
   b. Member has failed prior treatment with or is intolerant to previous osteoporosis therapy (i.e., oral bisphosphonates or injectable antiresorptive agents)

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

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

Pulmonary Arterial Hypertension

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:
   - mPAP ≥ 25 mmHg
   - PCWP ≤ 15 mmHg
   - 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:
   - Post cardiac surgery
   - Chronic heart disease
   - Chronic lung disease associated with prematurity
   - Congenital diaphragmatic hernia

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with PAH who are currently receiving Uptravi therapy through a paid pharmacy or medical benefit.

IV. APPENDIX

WHO Classification of Pulmonary Hypertension

WHO Group 1. Pulmonary Arterial Hypertension (PAH)

1.1 Idiopathic (IPAH)

1.2 Heritable PAH
1.2.1 Germline mutations in the bone morphogenetic protein receptor type 2 (BMPR2)
1.2.2 Activin receptor-like kinase type 1 (ALK1), endoglin (with or without hereditary hemorrhagic telangiectasia), Smad 9, caveolin-1 (CAV1), potassium channel super family K member-3 (KCNK3)
1.2.3 Unknown
1.3 Drug- and toxin-induced
1.4. 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’. Pulmonary veno-occlusive disease (PVOD) and/or pulmonary capillary hemangiomatosis (PCH)
1". Persistent pulmonary hypertension of the newborn (PPHN)

WHO Group 2. Pulmonary Hypertension Owing to Left Heart Disease
2.1 Systolic dysfunction
2.2 Diastolic dysfunction
2.3 Valvular disease
2.4 Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies

WHO Group 3. Pulmonary Hypertension Owing to Lung Disease and/or Hypoxia
3.1 Chronic obstructive pulmonary disease
3.2 Interstitial lung disease
3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
3.4 Sleep-disordered breathing
3.5 Alveolar hypoventilation disorders
3.6 Chronic exposure to high altitude
3.7 Developmental abnormalities

WHO Group 4. Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

WHO Group 5. Pulmonary Hypertension with Unclear Multifactorial Mechanisms
5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders, splenectomy
5.2 Systemic disorders: sarcoidosis, pulmonary Langerhans cell histiocytosis: lymphangioleiomyomatosis, neurofibromatosis, vasculitis
5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
5.4 Others: tumoral obstruction, fibrosing mediastinitis, chronic renal failure on dialysis, segmental PH

V. REFERENCES
PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

VIBERZI
(eluxadoline)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization
Ref# 1287-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
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
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).

The efficacy and safety of Viberzi in IBS-D patients was established in two randomized, multi-center, multi-national, double-blind, placebo-controlled trials (Studies 1 and 2). A total of 1281 patients in Study 1 and 1145 patients in Study 2 received treatment with Viberzi 75 mg, Viberzi 100 mg or placebo twice daily. Study 1 and Study 2 included identical 26-week double-blind, placebo-controlled treatment periods. Study 1 continued double-blinded for an additional 26 weeks for long-term safety (total of 52 weeks of treatment), followed by a 2-week follow-up. Study 2 included a 4-week single-blinded, placebo-withdrawal period upon completion of the 26-week treatment period. Efficacy of Viberzi was assessed in both trials using an overall composite responder primary endpoint. The primary endpoint was defined by the simultaneous improvement in the daily worst abdominal pain score by ≥30% as compared to the baseline weekly average and a reduction in the Bristol Stool Scale (BSS) to <5 on at least 50% of the days within a 12-week time interval.

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.

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

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### Mapping Instructions

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<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>Your plan covers this drug when you have irritable bowel syndrome with diarrhea. Your use of this drug does not meet the requirements. This is based on the information we have.</td>
</tr>
</tbody>
</table>
| 2. Deny | Approve, 36 months | 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 use of this drug does not meet these requirements. This is based on the information we have. |
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:

A. Genotype 1, 2, 3, 4, 5, or 6 infection and have previously been treated with an HCV regimen containing an NS5A inhibitor

B. 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

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

Authorization of up to 12 weeks total may be granted for members when either of the following criteria is met:

1. Member has genotype 1, 2, 3, 4, 5, or 6 infection and failed prior treatment with an HCV NS5A inhibitor-containing regimen

2. Member has genotype 1a or 3 infection and failed prior treatment with a sofosbuvir-containing regimen without an 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. REFERENCE

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 stage IV RCC
   2. Uterine sarcoma
   3. Soft tissue sarcoma of one of the following subtypes:
      a. Gastrointestinal stromal tumors (GIST)
      b. Angiosarcoma
      c. Pleomorphic rhabdomyosarcoma
      d. Retroperitoneal/intra-abdominal sarcoma
      e. Extremity/superficial trunk, head/neck sarcoma
   4. Medullary, papillary, Hürthle cell, or follicular thyroid carcinoma:
   5. Metastatic dermatofibrosarcoma protuberans (DFSP)
   6. Ovarian cancer
      a. Epithelial ovarian cancer
      b. Fallopian tube cancer
      c. Primary peritoneal cancer

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 and the member has ONE of the following subtypes of STS:
      a. Gastrointestinal stromal tumor (GIST)
      b. Pleomorphic rhabdomyosarcoma
PRIOR AUTHORIZATION CRITERIA

<table>
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<th>BRAND NAME</th>
<th>XENICAL (generic) (orlistat)</th>
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<tr>
<td>Status:</td>
<td>CVS Caremark Criteria</td>
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<tr>
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<td>Initial Prior Authorization</td>
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FDA-APPROVED INDICATIONS
Xenical is indicated for obesity management including weight loss and weight maintenance when used in conjunction with a reduced-calorie diet. Xenical is also indicated to reduce the risk for weight regain after prior weight loss. Xenical is indicated for obese patients with an initial body mass index (BMI) ≥30 kg/m² or ≥27 kg/m² in the presence of other risk factors (e.g., hypertension, diabetes, dyslipidemia).

COVERAGE CRITERIA
Xenical will be covered with prior authorization when the following criteria are met:
- The patient has taken the requested drug for a minimum of 6 months AND
  - The patient has lost at least 5 percent of baseline bodyweight or the patient has continued to maintain their weight loss
- OR
- The requested medication 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. Xenical is indicated for obesity management including weight loss and weight maintenance when used in conjunction with a reduced-calorie diet. Xenical is also indicated to reduce the risk for weight regain after prior weight loss. Xenical is indicated for obese patients with an initial body mass index (BMI) ≥30 kg/m² or ≥27 kg/m² in the presence of other risk factors (e.g., hypertension, diabetes, dyslipidemia). Xenical is contraindicated in pregnancy, patients with chronic malabsorption syndrome, and patients with cholestasis.

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 ≥ 30 kg/m² or ≥ 27 kg/m² if other risk factors are present (e.g., hypertension, diabetes, dyslipidemia, sleep apnea, cardiovascular disease).4-6

The National Heart, Lung, and Blood Institute recommends the initial goal of weight-loss therapy should be an approximately 10% reduction in body weight from baseline during the initial three to six months of therapy. With success, further weight loss can be attempted, if indicated, through further assessment. Maintenance therapy beyond six months of initial treatment may be considered for patients who have achieved at least an average of one pound per week of weight loss, or who have achieved a 5% reduction of the initial body weight over a 6 month period since the initiation of Xenical therapy.4-6

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 reevaluated with the patient and lack of long-term data is acknowledged.4-6
Clinical trials for up to four years duration have shown that Xenical improves cardiovascular risk factors and reduces diabetes incidence in high-risk individuals, thus it may be especially useful in patients at high risk for developing type 2 diabetes, with high LDL-cholesterol concentrations, or with pre-existing cardiovascular disease. Therefore, long-term use of Xenical will be considered for patients who demonstrate continued weight loss or maintenance of original weight loss.

REFERENCES
meter AND has additional risk factors?

5 Will the requested medication be used with a reduced calorie diet and increased physical activity?  

<table>
<thead>
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<th>Guidelines for Approval</th>
<th>12 Months</th>
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**Mapping Instructions**

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<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>Your plan covers this drug when you have lost at least 5 percent of your body weight or have continued to keep your weight loss off. Your use of this drug does not meet the requirement. This is based on the information we have.</td>
</tr>
<tr>
<td>2. Approve for 12 months</td>
<td>Deny</td>
<td>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 use of this drug does not meet the requirements. This is based on the information we have.</td>
</tr>
<tr>
<td>3. Go to 5</td>
<td>Go to 4</td>
<td></td>
</tr>
<tr>
<td>4. Go to 5</td>
<td>Deny</td>
<td>Your plan covers this drug when you will diet and exercise. Your use of this drug does not meet the requirement. This is based on the information we have.</td>
</tr>
<tr>
<td>5. Approve for 12 months</td>
<td>Deny</td>
<td></td>
</tr>
</tbody>
</table>
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.

A. FDA-Approved Indication

Xtandi is indicated for the treatment of patients with metastatic castration-resistant prostate cancer.

B. Compendial Uses

Prostate cancer:

1. Used as a single agent as secondary hormone therapy for progression or metastases following medical or surgical androgen deprivation therapy (ADT)
2. In combination with ADT
   i. As part of neoadjuvant/concomitant/adjuvant ADT to enhance effectiveness of radiation therapy
   ii. In ADT-naive patients for a minimum of 7 days in patients with overt metastases who are at risk of developing symptoms associated with androgen flare
   iii. Following inadequate testosterone suppression with ADT alone

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

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*  
(generic)  

 XYREM  
(sodium oxybate)  

Status: CVS Caremark Criteria  
Type: Initial Prior Authorization with Quantity Limit  
Ref # 254-C  

* 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
Xyrem oral solution is indicated for the treatment of cataplexy in narcolepsy.

Xyrem oral solution is indicated for the treatment of excessive daytime sleepiness (EDS) in narcolepsy.

Limitations of Use
Xyrem may only be dispensed to patients enrolled in the Xyrem REMS Program.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:
• The request is for continuation of Xyrem (sodium oxybate) AND the patient experienced a decrease in daytime sleepiness with narcolepsy or a decrease in cataplexy episodes with narcolepsy
  OR
• The diagnosis is confirmed by sleep lab evaluation
  AND
  o The requested drug is being prescribed for the treatment of cataplexy in narcolepsy
    OR
  o The requested drug is being prescribed for excessive daytime sleepiness in a patient with narcolepsy
    AND
      ▪ The patient experienced an inadequate treatment response or intolerance to at least one central nervous system (CNS) stimulant drug (e.g., amphetamine, dextroamphetamine, or methylphenidate) AND one central nervous system (CNS) promoting wakefulness drug (e.g., modafinil, armodafinil)
    OR
      ▪ The patient has a contraindication to at least one central nervous system (CNS) stimulant drug (e.g., amphetamine, dextroamphetamine, or methylphenidate) AND one central nervous system (CNS) wakefulness promoting drug (e.g., modafinil, 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. Xyrem oral solution is indicated for the treatment of cataplexy in narcolepsy and excessive daytime sleepiness (EDS) in narcolepsy.

Because of the risks of central nervous system depression and abuse/misuse, Xyrem is available only through a restricted distribution program called the Xyrem REMS Program. The Xyrem REMS Program required components are: medication is dispensed by a certified centralized pharmacy, prescribers must complete the enrollment forms and comply with the requirements, and patients must understand the risks and benefits of Xyrem.
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.4,5

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 Since Xyrem has risks associated with therapy and there are effective alternatives available, a trial of one central nervous system (CNS) promoting wakefulness drug (e.g., modafinil, armodafinil) and one central nervous system (CNS) stimulant drug (e.g., amphetamine, dextroamphetamine, or methylphenidate) will be required.

The guidelines state that the goal of therapy should be to produce the fullest possible return of normal function for patients.4,6 Therefore, if the request is for the continuation of Xyrem, it should be determined that the patient has experienced a decrease in daytime sleepiness with narcolepsy or a decrease in cataplexy episodes with narcolepsy.

The recommended starting dose of Xyrem is 4.5 grams (g) per night administered orally in two equal, divided doses: 2.25 g at bedtime and 2.25 g taken 2.5 to 4 hours later. The dose can be increased by 1.5 g per night at weekly intervals (additional 0.75 g at bedtime and 0.75 g taken 2.5 to 4 hours later) to the effective dose range of 6 g to 9 g per night orally. Doses higher than 9 g per night have not been studied and should not ordinarily be administered. Therefore, the approval will be limited to a maximum of three 180 milliliter (mL) bottles (540 mL) per month.

REFERENCES
**CRITERIA FOR APPROVAL**

1. Is this request for the continuation of Xyrem (sodium oxybate)?
   - Yes
   - No
   [If no, then skip to question 3.]

2. Has the patient experienced a decrease in daytime sleepiness with narcolepsy or a decrease in cataplexy episodes with narcolepsy?
   - Yes
   - No
   [If yes, then skip to question 8.]

3. Is the requested drug being prescribed for the treatment of cataplexy in narcolepsy?
   - Yes
   - No
   [If yes, then skip to question 7.]

4. Is the requested drug being prescribed for the treatment of excessive daytime sleepiness in a patient with narcolepsy?
   - Yes
   - No

5. Did the patient experience an inadequate treatment response or intolerance to at least one central nervous system (CNS) stimulant drug (e.g., amphetamine, dextroamphetamine, or methylphenidate) AND one central nervous system (CNS) promoting wakefulness drug (e.g., modafinil, armodafinil)?
   - Yes
   - No
   [If yes, then skip to question 7.]

6. Does the patient have a contraindication to at least one central nervous system (CNS) stimulant drug (e.g., amphetamine, dextroamphetamine, or methylphenidate) AND one central nervous system (CNS) wakefulness promoting drug (e.g., modafinil, armodafinil)?
   - Yes
   - No

7. Has the diagnosis been confirmed by sleep lab evaluation?
   - Yes
   - No

8. Does the patient require the use of more than the plan allowance of 540 milliliters (mL) per month (270 grams per month)?
   - Yes
   - No
   [Rph Note: If yes, then deny and enter a partial approval for 540 mL per 25 days.]

**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 8</td>
</tr>
<tr>
<td>3.</td>
<td>Go to 7</td>
</tr>
<tr>
<td>4.</td>
<td>Go to 5</td>
</tr>
</tbody>
</table>

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

- Your plan covers this drug when you meet one of these conditions:
  - You have a decrease in daytime sleepiness with narcolepsy
  - You have a decrease in cataplexy episodes with narcolepsy
  Your use of this drug does not meet the requirement. This is based on the information we have.

- Your plan covers this drug when you have one of these conditions:
  - Cataplexy with narcolepsy
  - Excessive daytime sleepiness with narcolepsy
  Your use of this drug does not meet the requirement. This is based on the information we have.
<table>
<thead>
<tr>
<th></th>
<th>Go to 7</th>
<th>Go to 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.</td>
<td>Go to 7</td>
<td>Deny</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Your plan covers this drug when you meet all of these conditions:</td>
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<tr>
<td></td>
<td></td>
<td>- You tried a central nervous system (CNS) stimulant drug (e.g., amphetamine, dextroamphetamine, or methylphenidate) and a central nervous system (CNS) wakefulness promoting drug (e.g., modafinil, armodafinil)</td>
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<td></td>
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<td>- These drugs did not work for you or you cannot take them</td>
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<td></td>
<td>Your use of this drug does not meet the requirements. This is based on the information we have.</td>
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<tr>
<td>7.</td>
<td>Go to 8</td>
<td>Deny</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Your plan covers this drug when you have had a sleep lab test.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Your use of this drug does not meet the requirement. This is based on the information we have.</td>
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<tr>
<td>8.</td>
<td>Deny</td>
<td>Approve, 12 months, 540 milliliters/month*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- 540 milliliters/month of Xyrem.</td>
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<tr>
<td></td>
<td></td>
<td>You have been approved for the maximum quantity that your plan covers. Your request for additional quantities of the requested drug and strength has been denied.</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

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.

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, 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.

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

II. REQUIRED INFORMATION

Testing or analysis confirming CD19 protein on the surface of the B-cell.

III. CRITERIA FOR INITIAL APPROVAL

Large B-cell lymphoma

Authorization of 3 months may be granted to members 18 years of age or older for treatment of large B-cell lymphoma (including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma) when all of the following criteria are met:

A. The disease is relapsed or refractory to treatment after two or more lines of therapy.
B. The member has not received a previous treatment course of Yescarta.
C. The member does not have primary central nervous system lymphoma.
D. The B-cells must be CD19-positive as confirmed by testing or analysis.

IV. 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

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 treatment of CRC.

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

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, etc.).

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

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

Zytiga is indicated in combination with prednisone for the treatment of patients with metastatic castration-resistant prostate cancer.

B. Compendial Uses

Zytiga can be used in combination with prednisone and androgen-deprivation therapy for the treatment of patients with newly diagnosed, metastatic, high-risk hormone-sensitive 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 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