Reference number(s)
2063-A

STANDARD MEDICARE PART B MANAGEMENT

NUCALA (mepolizumab)

POLICY

I. INDICATIONS

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

FDA-Approved Indications

1. Maintenance Treatment of Severe Asthma
   Nucala is an interleukin-5 antagonist monoclonal antibody (IgG1 kappa) indicated for add-on maintenance treatment of patients with severe asthma aged 6 years and older, and with an eosinophilic phenotype.

   Limitations of Use: Not for relief of acute bronchospasm or status asthmaticus

2. Eosinophilic Granulomatosis with Polyangiitis
   Nucala is indicated for the treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA).

3. Hypereosinophilic Syndrome
   Nucala is indicated for the treatment of adult and pediatric patients aged 12 years and older with hypereosinophilic syndrome (HES) for ≥6 months without an identifiable non-hematologic secondary cause.

4. Chronic rhinosinusitis with nasal polyps (CRSwNP)
   Nucala is indicated as add-on maintenance treatment of adult patients 18 years and older with chronic rhinosinusitis with nasal polyps (CRSwNP)

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. DOCUMENTATION

The following documentation must be available, upon request, for all submissions:

A. Asthma:
   1. For initial requests:
      i. Member's chart notes or medical record showing pretreatment blood eosinophil count, dependance on inhaled corticosteroids if applicable.
      ii. Chart notes, medical record documentation, or claims history supporting previous medications tried including drug, dose, frequency, and duration. If therapy is not advisable, documentation of clinical reason to avoid therapy.

2. For continuation requests: Chart notes or medical record documentation supporting improvement in asthma control.

B. EGPA:
1. For initial requests:
   i. Member's chart notes or medical record showing pretreatment blood eosinophil count
   ii. Chart notes, medical record documentation, or claims history supporting previous medications tried including drug, dose, frequency, and duration. If therapy is not advisable, documentation of clinical reason to avoid therapy.
2. For continuation requests: Chart notes or medical record documentation supporting improvement in EGPA control.

C. HES:
1. For initial requests:
   i. FIP1L1-PDGFRA fusion gene test results
   ii. Member's chart notes or medical record showing pretreatment blood eosinophil count
2. For continuation requests: Chart notes or medical record documentation supporting improvement in HES control.

D. CRSwNP:
1. For initial requests:
   i. Member's chart notes or medical record showing nasal endoscopy, anterior rhinoscopy, or computed tomography (CT) details (e.g., location, size), or Meltzer Clinical Score or endoscopic nasal polyp score (NPS) (where applicable).
   ii. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
2. For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

III. CRITERIA FOR INITIAL APPROVAL

A. Eosinophilic asthma

Authorization of 12 months may be granted for treatment of eosinophilic asthma when all of the following criteria are met:
1. Member is 6 years of age or older.
2. Member has a baseline blood eosinophil count (pretreatment with a biologic indicated for asthma) of at least 150 cells per microliter.
3. Member has a history of severe asthma despite current treatment with both of the following medications at optimized doses, unless the member has a clinical reason to avoid these therapies:
   i. Inhaled corticosteroid
   ii. Additional controller (i.e., long acting beta$_2$-agonist, long acting muscarinic antagonist, leukotriene modifier, or sustained release theophylline)
4. Member will not use the requested medication concomitantly with other biologics indicated for asthma (e.g., Cinqair, Dupixent, Fasenra, Tezspire, or Xolair).

B. Eosinophilic Granulomatosis with Polyangiitis

Authorization of 12 months may be granted for treatment of eosinophilic granulomatosis with polyangiitis when all of the following criteria are met:
1. Member is 18 years of age or older.
2. Member has a history or the presence of an eosinophil count of more than 1000 cells per microliter or a blood eosinophil level of greater than 10%.
3. Member is currently taking oral corticosteroids, unless contraindicated or not tolerated.

C. Hypereosinophilic Syndrome (HES)

Authorization of 12 months may be granted for treatment of hypereosinophilic syndrome (HES) when all of the following criteria are met:

1. Member is 12 years of age or older.
2. Member does not have either of the following:
   i. HES secondary to a non-hematologic cause (e.g., drug hypersensitivity, parasitic helminth infection, [human immunodeficiency virus] HIV infection, non-hematologic malignancy)
   ii. FIP1L1-PDGFRA kinase-positive HES
3. Member has a history or presence of a blood eosinophil count of at least 1000 cells per microliter.
4. Member has been on a stable dose of HES therapy (e.g., oral corticosteroid, immunosuppressive, and/or cytotoxic therapy).
5. Member has had HES for at least 6 months.

D. Chronic rhinosinusitis with nasal polyps

Authorization of 6 months may be granted for treatment of chronic rhinosinusitis with nasal polyps when all of the following criteria are met:

1. Member is 18 years of age or older
2. Member has bilateral nasal polyposis and chronic symptoms of sinusitis despite intranasal corticosteroid treatment for at least 2 months unless contraindicated or not tolerated; and
3. The member has CRSwNP despite one of the following:
   i. Prior sino-nasal surgery
   ii. Prior treatment with systemic corticosteroids within the last two years was ineffective, unless contraindicated or not tolerated
4. Member has one of the following:
   i. A bilateral nasal endoscopy, anterior rhinoscopy, or computed tomography (CT) showing polyps reaching below the lower border of the middle turbinate or beyond in each nostril
   ii. Meltzer Clinical Score of 2 or higher in both nostrils
   iii. A total endoscopic nasal polyp score (NPS) of at least 5 with a minimum score of 2 for each nostril
5. Member has symptom of nasal blockage, congestion, or obstruction plus one additional symptom:
   i. Rhinorrhea (anterior/posterior)
   ii. Reduction or loss of smell
   iii. Facial pain or pressure
6. Member will continue to use a daily intranasal corticosteroid while being treated with the requested medication, unless contraindicated or not tolerated.
7. Member will not use Nucala concomitantly with other biologics indicated for chronic rhinosinusitis with nasal polyps (e.g., Dupixent or Xolair).

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested medication.

A. Eosinophilic Asthma

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

1. Member is 6 years of age or older.
2. The member is currently receiving therapy with the requested medication.
3. Nucala is being used to treat an indication enumerated in Section III.
4. The member is receiving benefit from therapy as defined by reduction in the frequency and/or severity of symptoms and exacerbations.

5. Member will not use Nucala concomitantly with other biologics indicated for asthma (e.g., Cinqair, Dupixent, Fasenra, Tezspire, or Xolair).

B. Eosinophilic granulomatosis with polyangiitis

Authorization of 12 months may be granted for continuation of treatment of eosinophilic granulomatosis with polyangiitis when all of the following criteria are met:

1. Member is 18 years of age or older.
2. The member is currently receiving therapy with the requested medication.
3. The requested medication is being used to treat an indication enumerated in Section III.
4. The member is receiving benefit from therapy as defined by reduction in the frequency and/or severity of symptoms and exacerbations.

C. Hypereosinophilic syndrome (HES)

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

1. Member is 12 years of age or older.
2. The member is currently receiving therapy with the requested medication.
3. The requested medication is being used to treat an indication enumerated in Section III.
4. The member is receiving benefit from therapy as defined by reduction in the frequency and/or severity of symptoms and exacerbations.

D. Chronic rhinosinusitis with nasal polyps (CRSwNP)

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

1. Member is 18 years of age or older.
2. The member is currently receiving therapy with the requested medication.
3. The requested medication is being used to treat an indication enumerated in Section III.
4. The member is receiving benefit from therapy as defined by achieving or maintaining a positive clinical response with the requested medication as evidenced by improvement in signs and symptoms of CRSwNP (e.g., improvement in nasal congestion, nasal polyp size, loss of smell, anterior or posterior rhinorrhea, sinonasal inflammation, hyposmia and/or facial pressure or pain or reduction in corticosteroid use).
5. Member will not use the requested medication concomitantly with other biologics indicated for chronic rhinosinusitis with nasal polyps (e.g., Dupixent or Xolair).

V. SUMMARY OF EVIDENCE

The contents of this policy were created after examining the following resources:

1. The prescribing information for Nucala.
2. The available compendium
    a. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    b. Micromedex DrugDex
    c. American Hospital Formulary Service- Drug Information (AHFS-DI)
    d. Lexi-Drugs
3. Global Initiative for Asthma (GINA): Global strategy for asthma management and prevention
4. National Asthma education and Prevention Program Expert Panel 3: Guidelines for the diagnosis and management of asthma
5. Managing asthma in adolescents and adults: 2020 asthma guideline update from the National Asthma Education and Prevention Program
6. EAACI biologicals guidelines- recommendations for severe asthma

7. American College of Rheumatology/Vasculitis Foundation Guideline for the management of antineutrophil cytoplasmic antibody-associated vasculitis
8. European Position Paper on Rhinosinusitis and Nasal Polyps

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Nucala are covered.

VI. EXPLANATION OF RATIONALE

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for using Nucala for allergic asthma can be found in the manufacturer's prescribing information, the Global Initiative for Asthma (GINA): Global strategy for asthma management and prevention guidelines, and the guideline update from the National Asthma Education and Prevention Program. The prescribing information indicates the minimum labeled age for Nucala is six years of age. Nucala should be used in patients whose symptoms are inadequately controlled with inhaled corticosteroids. According to the 2022 update of the GINA Global Strategy for asthma management and prevention, Nucala should be considered as an add-on therapy that is uncontrolled on other medications such as long-acting beta2-agonists, leukotriene receptor antagonists, tiotropium, or inhaled corticosteroids-formoterol maintenance and reliever therapy (MART).

According to the EAACI biologicals guidelines, Nucala should be given as add-on therapy in adults and pediatric patients 12 years and older with uncontrolled severe eosinophilic asthma (blood eosinophil cell counts 300 cells/mcL or more in the past 12 months or 150 cells/mcL or more at initiation) to decrease severe asthma exacerbations (strong recommendation for adults; conditional for pediatric patients), decrease or withdraw corticosteroids (strong recommendation for adults; conditional for pediatric patients), and improve lung function (may be relevant in severe asthma with very low lung function), quality of life, and asthma control (conditional recommendation for all).

Support for using Nucala to treat eosinophilic granulomatosis with polyangiitis can be found in a study by Wechsler et al. In adults with relapsing or refractory eosinophilic granulomatosis with polyangiitis (EGPA), a randomized trial (N=136) evaluated the addition of mepolizumab versus placebo to stable doses of prednisoLONE or predniSONE with or without additional immunosuppressive therapy. Enrolled participants were at least 18 years of age, had received a diagnosis of relapsing or refractory eosinophilic granulomatosis with polyangiitis at least 6 months previously, and had been taking a stable dose of prednisolone or prednisone (≥7.5 to ≤50.0 mg per day, with or without additional immunosuppressive therapy) for at least 4 weeks before the baseline visit. Eosinophilic granulomatosis with polyangiitis was defined as a history or presence of asthma, a blood eosinophil level of 10% or an absolute eosinophil count of more than 1000 cells per cubic millimeter, and the presence of two or more criteria that are typical of eosinophilic granulomatosis with polyangiitis. Nucala was given as a 300mg subcutaneous injection every 4 weeks. In co-primary outcomes, the total accrued weeks of remission over 52 weeks was significantly greater with mepolizumab versus placebo (OR, 5.91; 95% CI, 2.68 to 13.03) and remission at both week 36 and 48 was also significantly improved (32% vs 3%; OR, 16.74; 95% CI, 3.61 to 77.56). Remission for at least 24 weeks was achieved in 28% with Nucala and 3% with placebo; although, in subgroup analyses, the outcome was not significantly different with Nucala versus placebo in patients with an absolute eosinophil count (AEC) less than 150/mm(3) (n=57; 21% vs 7%) but was significantly greater with Nucala in patients with an AEC of 150/mm(3) or greater (n=79; 33% vs 0%). Remission within the first 23 weeks that continued until week 52 (secondary outcome) was also significantly greater with Nucala (19% vs 1%). Remission was defined as a Birmingham Vasculitis Activity Score (BVAS) of 0 (on a 63-point scale) and a prednisoLONE/predniSONE dose of 4 mg/day or less. The time to first relapse was significantly reduced with Nucala versus placebo (HR, 0.32; 95% CI, 0.21 to 0.5); a relapse within the 52-week study period was reported in 56% with Nucala and 82% with placebo (major

relapses, 22% vs 35%). The annualized relapse rate was significantly reduced with Nucala (1.14 vs 2.27). Relapses with Nucala and placebo, respectively, were vasculitis (43% and 65%), asthma (37% and 60%), and sinonasal (35% and 51%). Relapse was defined as active vasculitis (BVAS greater than 0), active asthma signs or symptoms and a worsening Asthma Control Questionnaire score, or active nasal or sinus disease with worsening in at least 1 of the sinonasal-symptom items leading to an increase in glucocorticoid dose to more than 4 mg/day of prednisoLONE (or equivalent), initiation of or increase in immunosuppressive therapy, or hospitalization. During weeks 48 through 52, the average prednisoLONE/predniSONE dose was significantly reduced with Nucala versus placebo (OR, 0.2; 95% CI, 0.09 to 0.41), a dosage of 4 mg/day or less was achieved in 44% versus 7%, and discontinuation was achieved in 18% versus 3%. Over the 52-week study period, the mean daily dose was 9.2 mg with mepolizumab and 13.5 mg with placebo. Adverse events were reported in 97% with Nucala and 94% with placebo and included headache (32% vs 18%), nasopharyngitis (18% vs 24%), arthralgia (22% vs 18%), sinusitis (21% vs 16%), and upper respiratory tract infection (21% vs 16%). Serious adverse events were reported in 18% with Nucala and 26% with placebo and included exacerbation or worsening of asthma (3% vs 6%).

Support for using Nucala to treat hypereosinophilic syndrome (HES) can be found in the prescribing information. Nucala compared with placebo significantly reduced HES flares at 32 weeks (28% vs 56%; OR, 0.28; 95% CI, 0.12 to 0.64) in a randomized, double-blind trial (N=108) of adults and adolescents. HES flares were defined as worsening of clinical HES signs and symptoms or increasing eosinophils on at least 2 occasions that resulted in the need to increase oral corticosteroids or increase/add cytotoxic or immunosuppressive therapy. Nucala (300 mg every 4 weeks) versus placebo was also associated with significant reductions in the annualized rate of HES flares (0.5 vs 1.46; RR, 0.34; 95% CI, 0.19 to 0.63), HES flares during week 20 through week 32 (17% vs 35%; OR, 0.33; 95% CI, 0.13 to 0.85), and change from baseline in the median Brief Fatigue Inventory Item 3 score (-0.66 vs +0.32 on a 10-point scale). Patients were 12 years or older (mean age, 46 years) and had HES for at least 6 months (mean duration, 5.55 years). They experienced at least 2 HES flares in the past year (worsening of clinical symptoms or blood eosinophil counts that required an escalation in therapy) and had a blood eosinophil count of 1000 cell/mcL or higher during screening. All patients were on stable HES therapy for at least 4 weeks before randomization, which could include chronic or episodic oral corticosteroids, immunosuppressive, or cytotoxic therapy. Patients with nonhematologic secondary HES or FIP1L1-PDGFR-alpha kinase-positive HES were excluded.

Support for using Nucala to treat chronic rhinosinusitis can be found in the prescribing information. The addition of mepolizumab versus placebo to standard of care significantly improved the change from baseline to week 52 in total endoscopic nasal polyp score (median change, -1 vs 0 on an 8-point scale; difference, -0.73; 95% CI, -1.11 to -0.34) and nasal obstruction visual analog scale (VAS) score (median change, -4.41 vs -0.82 on a 10-point scale; difference, -3.14; 95% CI, -4.09 to -2.18) in the randomized SYNAPSE trial (N=407). The study enrolled adults with recurrent, refractory, severe, bilateral nasal polyp symptoms despite standard of care treatment who were eligible for repeat nasal surgery. Nucala significantly reduced the proportion of patients who required nasal surgery (9% vs 23%) and who required systemic corticosteroids (25% vs 37%). The change in the following scores were also significantly reduced with Nucala: overall symptom VAS score (-4.48 vs -0.9), Sino-Nasal Outcome Test (SNOT)-22 total score (-30 vs -14), composite VAS score (combined nasal obstruction, nasal discharge, throat mucus, and loss of smell scores; -3.96 vs -0.89) and smell VAS score (-0.53 vs 0). Adverse events reported more frequently with Nucala included nasopharyngitis (25% vs 23%), oropharyngeal pain (8% vs 5%), and arthralgia (6% vs 2%). Patients had at least 1 nasal surgery in the past 10 years and required stable maintenance therapy with mometasone furoate intranasal spray for at least 8 weeks before screening.

VII. REFERENCES

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