mepolizumab (Nucala®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO046

Description

Mepolizumab (Nucala) is a subcutaneously administered monoclonal antibody (IgG1 Kappa) that antagonizes interleukin-5 (IL-5).

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity limits

Product Name	Dosage Form	Indication	Quantity Limit
mepolizumab (Nucala)	100 mg/mL syringe, 100 mg/mL autoinjector	Asthma (severe)	1 syringe/autoinjector/28 days
		Eosinophilic granulomatosis with polyangiitis	3 syringes/autoinjectors/28 days
		Hypereosinophilic Syndrome	3 syringes/autoinjectors/28 days

Initial Evaluation

I. Mepolizumab (Nucala) may be considered medically necessary when the following criteria below are met:
   A. Medication is prescribed by, or in consultation with, a dermatologist or a physician specializing in allergy, pulmonology, immunology, or ENT (ear, nose, throat); **AND**
   B. Must not be used in combination with another monoclonal antibody (e.g., benralizumab, dupilumab, omalizumab, reslizumab, etc.); **AND**
   C. A diagnosis of one of the following:
      1. **Asthma (severe)**; **AND**
         i. Member is six years of age or older; **AND**
         ii. Member has **SEVERE** asthma as defined by one of the following:
            a. Symptoms throughout the day
            b. Nighttime awakenings, often 7x/week
            c. SABA (e.g. albuterol, levalbuterol) use for symptom control occurs several times per day
            d. Extremely limited normal activities
            e. Lung function (percent predicted FEV1) <60%
            f. Exacerbations requiring oral systemic corticosteroids are generally more frequent and intense relative to moderate asthma; **AND**

iii. Member must have asthma with an eosinophilic phenotype defined as blood eosinophils ≥300 cells/µL within previous 12 months OR ≥150 cells/µL within 6 weeks of dosing; **AND**

iv. Member must have two or more exacerbations in the previous year requiring daily oral corticosteroids for at least 3 days (in addition to the regular maintenance therapy defined below); **AND**

v. Member is currently being treated with:

a. A medium- to high-dose, or maximally tolerated inhaled corticosteroid (ICS) [e.g., budesonide, fluticasone, mometasone]; **AND**

i. One additional asthma controller medication (e.g., long-acting beta-2 agonist [LABA] {e.g., Serevent Diskus}, long-acting muscarinic antagonist [LAMA] {e.g., Spiriva Respimat}, leukotriene receptor antagonist [e.g., Singular], or theophylline); **OR**

b. A maximally tolerated ICS/LABA combination product (e.g., Advair, Airduo, Breo, Dulera, Symbicort); **AND**

vi. Background controller medications (e.g., Advair, Airduo, Breo, Dulera, Symbicort) will be continued with the use of mepolizumab (Nucala), unless contraindicated; **OR**

2. **Eosinophilic Granulomatosis with Polyangiitis (EGPA)**; **AND**

i. Member is 18 years of age or older; **AND**

ii. Member has a confirmed diagnosis of EGPA (aka Churg-Strauss Syndrome) as defined by ALL of the following:

a. History or presence of asthma; **AND**

b. Blood eosinophil level 10% or an absolute eosinophil count >1000 cells/mm3; **AND**

c. TWO or more of the following:

i. Histopathologic evidence of eosinophilic vasculitis, perivascular eosinophilic infiltration or eosinophil rich granulomatous inflammation

ii. Neuropathy

iii. Pulmonary infiltrates

iv. Sinonasal abnormalities

v. Cardiomyopathy

vi. Glomerulonephritis

vii. Alveolar hemorrhage

viii. Palpable purpura

ix. Antineutrophil Cytoplasmic Antibody (ANCA) positivity; **AND**

iii. Member must have blood eosinophils ≥150 cells/µL within 6 weeks of dosing; **AND**

iv. Member has been on stable doses of concomitant oral corticosteroid therapy for at least 4 weeks (i.e., prednisone or prednisolone at a dose of 7.5 mg/day); **AND**

v. Physician has assessed baseline disease severity utilizing an objective measure/tool (e.g., Birmingham Vasculitis Activity Score [BVAS], history of asthma symptoms and/or exacerbations duration of remission or rate of relapses, etc.); **OR**

3. **Hypereosinophilic Syndrome (HES); AND**

i. Member is 12 years of age or older; **AND**

ii. Provider attests to ALL of the following:

a. Member has been diagnosed with HES for at least 6 months prior to starting treatment; **AND**

b. Member is confirmed to have F1P1L1-PDGFRα kinase-negative disease; **AND**

c. Member does NOT have non-hematologic secondary HES (e.g., drug hypersensitivity, parasitic helminth infection, HIV infection, non-hematologic malignancy); **AND**

d. Background HES therapy will be continued with the use of mepolizumab (Nucala), unless contraindicated; **AND**

iii. Member must have ALL of the following:

a. Two or more HES flares (see Supporting Evidence below) in the previous year; **AND**

b. Blood eosinophils ≥1000 cells/µL within 4 weeks of dosing; **AND**

c. Has been on stable doses of at least one other HES therapy (e.g., oral corticosteroids, immunosuppressive agents [hydroxyurea, cyclosporine, methotrexate, tacrolimus, azathioprine], cytotoxic therapy [imatinib], etc) for at least 4 weeks.

II. Mepolizumab (Nucala) is considered investigational when used for all other conditions, including but not limited to:

A. Non-severe, non-eosinophilic phenotype asthma

B. GPA (Wegener's granulomatosis) with polyangiitis

C. MPA (microscopic polyangiitis)

D. HES (hypereosinophilic syndrome) with F1P1L1-PDGFRα kinase-positive disease

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**

II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**

III. Must not be used in combination with another monoclonal antibody (e.g., benralizumab, dupilumab, omalizumab, reslizumab, etc.); **AND**

IV. A diagnosis of one of the following:

- **Asthma (severe); AND**
  - i. Member has exhibited improvement or stability of disease symptoms (e.g., reduced asthma exacerbations, FEV1, reduced systemic corticosteroid requirements, reduced hospitalizations); **AND**
  - ii. Background controller medications (e.g., Advair, Airduo, Breo, Dulera, Symbicort) will be continued with the use of mepolizumab (Nucala), unless contraindicated; **OR**
- **Eosinophilic Granulomatosis with Polyangiitis; AND**
  - i. Member has exhibited improvement or stability of disease symptoms as evidenced in one or more of the following:
    1. Member is in remission [defined as a Birmingham Vasculitis Activity Score (BVAS) score=0 and a prednisone/prednisolone daily dose of ≤ 7.5 mg]
    2. Decrease in maintenance dose of systemic corticosteroids
    3. Improvement in BVAS score compared to baseline
    4. Improvement in asthma symptoms or asthma exacerbations
    5. Improvement in duration of remission or decrease in the rate of relapses; **OR**
- **Hypereosinophilic Syndrome; AND**
  - i. Member has exhibited improvement or stability of disease symptoms (e.g., reduction in HES flares, improved fatigue, reduced oral corticosteroid requirements, decreased eosinophil levels)

Supporting Evidence

I. There is a lack of evidence supporting treatment with dual use of biologic therapies and a potential for increased risk of side effects.

II. Mepolizumab (Nucala) is indicated as an add-on maintenance treatment for members 6 years and older with a diagnosis of severe eosinophilic asthma (SEA), treatment for adult members

with eosinophilic granulomatosis with polyangiitis, and treatment for members 12 years and older with hypereosinophilic syndrome for at least 6 months without an identifiable non-hematologic secondary cause. The age expansion approval by the FDA from 12 years of age to 6 years of age in children with a diagnosis of SEA was based on an open-label study that was conducted in children age 6 to 11 years of age with SEA. In this study, pharmacokinetics, pharmacodynamics, and long-term safety were evaluated and determined consistent with the known safety profile associated with members aged 12 years and older.

III. The FDA approval of mepolizumab (Nucala) in the setting of severe eosinophilic asthma were evaluated in 3 randomized, placebo controlled, multicenter trials of 24 to 52 weeks in duration. The primary outcome was the rate of exacerbation, and it was reduced by 47% (95% confidence interval [CI], 28 to 60) among members receiving intravenous mepolizumab and by 53% (95% CI, 36 to 65) among those receiving subcutaneous mepolizumab, as compared with those receiving placebo (P<0.001 for both comparisons). The members enrolled in this trial were 12 to 82 years of age.

- Trial inclusion criteria required patients to have a history of 2 or more exacerbations requiring systemic corticosteroids in the previous year despite regular use of high-dose ICS plus additional controller(s) with or without oral corticosteroids (OCS). Patients were required to have at least 1 of the following 4 prespecified criteria in the previous 12 months: blood eosinophil count ≥300 cells/mcL, sputum eosinophil count ≥3%, exhaled nitric oxide concentration ≥50 ppb, or deterioration of asthma control after ≤25% reduction in regular maintenance ICS/OCS.

IV. The FDA approval of mepolizumab (Nucala) in the setting of eosinophilic granulomatosis with polyangiitis was evaluated in a multicenter, double-blind, parallel-group, phase 3 trial. The two primary end points were the accrued weeks of remission over a 52-week period, according to categorical quantification, and the proportion of participants in remission at both week 36 and week 48. In the mepolizumab treatment arm, there was significantly more accrued weeks of remission than placebo (28% vs. 3% of the participants had ≥24 weeks of accrued remission; odds ratio, 5.91; 95% confidence interval [CI], 2.68 to 13.03; P<0.001) and a higher percentage of participants in remission at both week 36 and week 48 (32% vs. 3%; odds ratio, 16.74; 95% CI, 3.61 to 77.56; P<0.001). The members that were enrolled in this trial were at least 18 years of age.

V. The FDA approval of mepolizumab (Nucala) in the setting of hypereosinophil syndrome was evaluated in a phase 3, randomized, double-blind, placebo-controlled, parallel-group, multicenter trial. Patients were randomized 1:1 to receive mepolizumab (Nucala) or placebo, plus an existing HES therapy. The primary endpoint evaluated the proportion of patients who experienced a flare during the 32-week study period compared to placebo, which was 28% compared to 56% (OR 0.28, 95% CI 0.12- 0.64, p=0.002). The patients enrolled in this trial were at least 12 years of age.

- Trial inclusion criteria required patients to have F1P1L1-PDGFRA-negative HES for at least 6 months, uncontrolled HES (defined as a history of at least 2 flares within the past 12 months and blood eosinophil count >1500 cells/µL and/or tissue eosinophilia), blood eosinophil count >1000 cells/µL, on stable background HES therapy (includes, but not limited to, oral corticosteroid [OCS], immunosuppressive, and/or cytotoxic therapy) for at least 4 weeks before randomization.
- HES flare defined as:
    i. An HES-related clinical manifestation, based on a physician-documented change in clinical signs or symptoms, necessitating an increase in the maintenance OCS dose >10 mg prednisone equivalent/day for 5 days OR an increase in/addition of any cytotoxic and/or immunosuppressive HES therapy; OR
    ii. Receipt of 2+ courses of blinded OCS during the treatment period

VI. The Global Initiative for Asthma (GINA) 2020 update recommends the addition of respiratory biologics, with respect to their allergic biomarkers, after inadequate asthma control despite good adherence and inhaler technique on maximized Step 4 (medium dose ICS-LABA) or Step 5 (high dose ICS-LABA) therapy. Other controller options for Step 4 include high dose ICS-LABA or add-on tiotropium, or add-on LTRA. Other controller options for Step 5 include add-on anti-IL5, or add-on low dose OCS, though guidelines note to consider side effects.

Investigational or Not Medically Necessary Uses

I. Mepolizumab (Nucala) has not been adequately studied for the following conditions and does not have established safety and efficacy in these populations:
    A. Non-severe, non-eosinophilic phenotype asthma
        i. Mepolizumab (Nucala) has not been studied in members with non-severe, non-eosinophilic phenotype asthma; therefore, it would be considered investigational when Nucala is requested in that setting.
    B. GPA (Wegener's granulomatosis) with polyangiitis and MPA (microscopic polyangiitis)
        i. Both GPA and MPA diagnoses were excluded in the phase 3 trial (A Study to Investigate Mepolizumab in the Treatment of Eosinophilic Granulomatosis with Polyangiitis).
    C. HES (hypereosinophilic syndrome) with F1P1L1-PDGFRα kinase-positive disease
        i. Mepolizumab (Nucala) has not been studied in members with F1P1L1-PDGFRα kinase-positive disease; therefore, it would be considered investigational when Nucala is requested in this setting.

References

1. Nucala [Prescribing Information]. Philadelphia, PA: GlaxoSmithKline LLC. Updated Sept 2020. Accessed Jan 2021.
2. Ortega HG, Liu MC, Pavord ID, et al. Mepolizumab Treatment in Members with Severe Eosinophilic Asthma. N Engl J Med 2014; 371:1198-1207. DOI: 10.1056/NEJMoa1403290.
3. Wechsler ME, Akuthota P, Jayne D, et al. Mepolizumab or Placebo for Eosinophilic Granulomatosis with Polyangiitis. N Engl J Med 2017; 376:1921-1932. DOI: 10.1056/NEJMoa1702079.
4. Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention. 2020 Update. Available from: http://www.ginasthma.org. Accessed January 2021.
5. Roufosse F, Kahn JE, Rothenberg ME, et al. Efficacy and safety of mepolizumab in hypereosinophilic syndrome: A phase III, randomized, placebo-controlled trial. *J Allergy Clin Immunol* 2020;146(6):1397-1405. DOI: 10.1016/j.jaci.2020.08.037.

Policy Implementation/Update:

Action and Summary of Changes	Date
Policy updated to reflect the new HES indication. Updated renewal length of authorization from 6 month to 12 months. Also added prescribed by or in consultation with a specialist requirement. For initial criteria: asthma: revised "severe eosinophilic asthma" verbiage to "asthma (severe)" in attempts to align with other respiratory biologic policies, revised verbiage for add-on maintenance treatment requirements to medium- to high-dose, or maximally tolerated ICS and one additional asthma controller medication OR maximally tolerated ICS/LABA combination, added requirement of continued use with background controller medications. For renewal criteria: removed criteria requirement confirming lack of toxicity to therapy; added "member has received a previous prior authorization approval for this agent through this health plan; AND member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise."; asthma: reformatted renewal criteria and added member exhibition of "stability" in addition to improvement of disease symptoms, added environmental triggers and continued background controller medications for asthma renewal criteria; EPGA: updated verbiage to "member has exhibited improvement or stability of disease symptoms". For supporting evidence: for asthma, added trial inclusion criteria and GINA 2020 guideline recommendations.	03/2021
Policy updated to reflect the newly approved age expansion for SEA from members 12 years and older to 6 years or older. Also added leukotriene modifiers as an example of a controller medication per GINA guidelines. To the EGPA section, examples of an objective measure/tool were added to align with renewal criteria and changed classification criteria for eosinophils to > 10% per ACR classification.	10/2019
New Policy	06/2019