Nucala

Mepolizumab meets member benefit certificate primary coverage criteria that there be scientific evidence of effectiveness in improving health outcomes when **ALL** the following criteria are met:

Severe Eosinophilic Asthma

INITIAL APPROVAL STANDARD REVIEW for up to 6 months:

1. Individual is 6 years of age or older; **AND**
2. Individual has a diagnosis of severe eosinophilic asthma; **AND**
3. *Evidence of asthma as demonstrated by both of the following (GINA, 2022):
    a. A pretreatment forced expiratory volume in 1 second (FEV1) < 80% predicted for adults or ≤ 90% for children (<18 years of age); **AND**
    b. Positive bronchodilator responsiveness test evidenced by an increase in FEV1 of > 12% and > 200 mL for adults and >12% for children (<18 years of age); **AND**

4. Documentation of inadequate control of symptoms with use of one of the following combination therapies (ERS/ATS, 2014), unless the individual is intolerant of, or has a medical contraindication to these agents:
    a. 3 months of high-dose inhaled corticosteroid (ICS) (equivalent to those defined in the policy guidelines) given in combination with a minimum of 3 months of controller medication (either a long-acting beta2-agonist [LABA], **OR** leukotriene receptor antagonist [LTRA], or theophylline); **OR**
    b. 6 months of ICS with daily oral glucocorticoids; **AND**

5. Individual has a blood eosinophil count of ≥ 150 cells/microliter at baseline prior to other eosinophil lowering therapy (e.g., systemic corticosteroids) and (in the absence of other potential causes of eosinophilia, including hypereosinophilic syndromes, neoplastic disease, and known or suspected parasitic infection) (Albers, 2019):
6. Individual has one of the following (ERS/ATS, 2014):
    a. A history of 2 or more exacerbations in the previous year, requiring bursts of systemic steroids (> 3 days each); **OR**
    b. b. At least one exacerbation requiring hospitalization, ICU stay or mechanical ventilation in the previous year; **AND**

7. Individual will continue to use maintenance asthma treatments (e.g., inhaled corticosteroid, LABA, LTRA or theophylline) in combination with mepolizumab; **AND**
8. Individual is not being treated concurrently with another biologic agent for the same or similar condition (such as benralizumab, dupilumab, omalizumab, reslizumab or tezepelumab); **AND**
9. Must be dosed in accordance with the FDA label; **AND**
10. Must be prescribed by or in consultation with an Allergist/Immunologist or Pulmonologist.

***FeNO testing is non-covered and is not considered adequate for establishing the diagnosis of asthma. Please see AR policy 2005020**

CONTINUED APPROVAL for up to 1 year:

1. Treatment with mepolizumab has resulted in clinical improvement as documented by one or more of the following:
   a. Decreased utilization of rescue medications; **OR**
   b. Decreased frequency of exacerbations (defined as worsening of asthma that requires an increase in ICS dose or treatment with systemic corticosteroids), hospitalizations, and/or ER/urgent visits; **OR**
   c. Increase in predicted FEV1 from pretreatment baseline; **AND**
2. Must be dosed in accordance with the FDA label.

Eosinophilic Granulomatosis with Polyangiitis

INITIAL APPROVAL STANDARD REVIEW for up to 6 months:

1. Individual is 18 years of age or older; **AND**
2. Individual is diagnosed with relapsing or refractory eosinophilic granulomatosis with polyangiitis for 6 months or greater, defined as:
   a. A history or presence of asthma; **AND**
   b. A blood eosinophil level of greater than or equal to 10% of leucocytes **or** an absolute eosinophil count of greater than 1000 cells per cubic millimeter (mm3); **AND**
   c. The presence of **two or more** features of eosinophilic granulomatosis with polyangiitis such as:
      a. A biopsy showing histopathological evidence of eosinophilic vasculitis, perivascular eosinophilic infiltration, or eosinophil-rich granulomatosis inflammation;
      b. Neuropathy, mono or poly [motor deficit or nerve conduction abnormality];
      c. Pulmonary infiltrates, non-fixed;
      d. Sino-nasal abnormality;
      e. Cardiomyopathy;
      f. Glomerulonephritis;
      g. Alveolar hemorrhage;
      h. Palpable purpura, **or**
      i. Antineutrophil cytoplasmic antibody [ANCA] positive status
3. Individual is currently taking oral corticosteroids and has been maintained on therapy for a minimum of 4 weeks, unless contraindicated or not tolerated; **AND**
4. Individual has had at least one relapse (i.e., requiring increase in oral corticosteroid dose, initiation/increased dose of immunosuppressive therapy or hospitalization within 2 years prior to starting treatment with the requested medication or has a refractory disease.

CONTINUED APPROVAL for up to 1 year:

1. Treatment with mepolizumab has resulted in clinical improvement as documented by the achievement of remission at some point during treatment, defined as one of the following:
   1. A reduction in the frequency of relapses;
   2. A reduction or discontinuation of daily oral corticosteroid dose;
   3. No active vasculitis; **AND**

2. Must be dosed in accordance with the FDA label.

Hypereosinophilic Syndrome (HES)

INITIAL APPROVAL STANDARD REVIEW for up to 6 months:

1. Individual is 12 years of age and older; **AND**
2. Individual is diagnosed with hypereosinophilic syndrome for > 6 months without an identifiable non hematologic secondary cause; **AND**
3. Individual is FIP1L1-PDGFRA negative (Roufosse 2020); **AND**

4. Individual has experienced 2 or more flares in the previous 12 months as defined by (Roufosse 2020):
    a. Worsening of HES-related symptoms; **AND**
    b. Blood eosinophil count requiring therapeutic escalation; **AND**

5. A blood eosinophil level >1000 cells/microliter uL on two examinations (at least one month apart) (Roufosse 2020); **AND**
6. Must be dosed in accordance with the FDA label.

CONTINUED APPROVAL for up to 1 year:

1. Treatment with mepolizumab has resulted in clinical improvement as documented by (Roufosse, 2020):
    a. Decreasing HES-related clinical symptoms; **OR**
    b. Decrease in number of flares; **AND**

2. Must be dosed in accordance with the FDA label.

Chronic Rhinosinusitis with Nasal polyposis (CRSwNP)

INITIAL APPROVAL STANDARD REVIEW for up to 6 months:

1. Individual is 18 years of age or older; **AND**
2. Individual is diagnosed with CRSwNP; **AND**
3. Mepolizumab is prescribed by a physician with expertise in the treatment of CRSwNP, e.g., an otolaryngologist [ear, nose, and throat (ENT) specialist] or an allergist/immunologist; **AND**
4. Individual has moderate to severe symptoms of nasal obstruction; **AND**

5. Individual has one of the following:
    a. Rhinorrhea; **OR**
    b. Decreased sense of smell for at least 12 weeks; **AND**

6. Individual has bilateral sinonasal polyposis reaching the lower border of the middle turbinate or beyond, which has been confirmed by nasal endoscopy, anterior rhinoscopy, or sinus CT scan (AAO-HNSF, 2015); **AND**
7. Individual has had at least one prior sinonasal surgery for CRSwNP or is not a candidate for sinonasal surgery to remove polyps – reason(s) for non-candidacy must be provided (AAO-HNS, 2015 and Al-Ahmad, 2022); **AND**
8. Individual has tried and failed systemic corticosteroids, unless contraindicated, in the past 2 years (AAAAI/ACAAI 2014); **AND**
9. Individual has tried and failed (e.g., lack of significant reduction in size or resolution of nasal

polyps), within the last 6 months, at least 8 weeks of continuous treatment with an intranasal corticosteroid post-sinonasal surgery (individuals who are ineligible for sinonasal surgery are still required to have tried intranasal corticosteroids) (AAO-HNS, 2015); **AND**
10. Individual will be using a daily intranasal corticosteroid during treatment with mepolizumab, unless contraindicated or not tolerated; **AND**
11. Individual is not being treated concurrently with a biologic agent for the same or similar condition (such as benralizumab, dupilumab, or omalizumab); **AND**
12. Must be dosed in accordance with the FDA label.

CONTINUED APPROVAL for up to 1 year:

Requirement of documentation in the medical records that the member has achieved and maintains a clinically meaningful benefit as defined below:

1. Individual has had improvement in clinical signs and symptoms of the disease (including but not limited to improvement in nasal polyp score or nasal congestion score); **AND**
2. Individual meets all of the following initial approval criteria:
    1. Mepolizumab is prescribed by a physician with expertise in the treatment of CRSwNP, e.g., an otolaryngologist [ear, nose, and throat (ENT) specialist] **OR** an allergist/immunologist; **AND**
    2. The individual will be using a daily intranasal corticosteroid during treatment with mepolizumab, unless contraindicated or not tolerated; **AND**
    3. Individual is not being treated concurrently with a biologic agent for the same or similar condition (such as benralizumab, dupilumab, or omalizumab); **AND**

3. Must be dosed in accordance with the FDA label.

Dosage and Administration
Mepolizumab is administered as a subcutaneous injection.

Please refer to the FDA label for dosing.

Policy Guidelines
The ERS/ATS definition of high doses of various inhaled glucocorticoids in relation to patient age (in mcg/day):

Age 6 to 12 years
Beclomethasone ≥ 320 (HFA MDI)
Budesonide ≥ 800 (MDI or DPI); (≥ 720 mcg/day of US labeled budesonide DPI)
Ciclesonide ≥ 160 (HFA MDI)
Fluticasone propionate ≥ 500 (HFA MDI or DPI); (≥ 440 mcg/day of US labeled fluticasone HFA MDI)
Mometasone ≥ 500 (DPI); (≥ 550 mcg/day of US labeled mometasone DPI)

Age >12 years
Beclomethasone ≥ 1000 (HFA MDI)
Budesonide ≥ 1600 (MDI or DPI) ;(≥ 1440 mcg/day of US labeled budesonide DPI)

Ciclesonide ≥ 320 (HFA MDI)
Fluticasone propionate ≥ 1000 (HFA MDI or DPI); (≥ 880 mcg/day of US labeled fluticasone HFA MDI)
Mometasone ≥ 800 (DPI); (≥ 880 mcg/day of US labeled mometasone DPI

Note: Designation of high doses is provided from manufacturers' recommendations where possible. Equivalent high doses may be expressed differently between countries and some products (e.g., beclomethasone) are available in multiple formulations with different dosing recommendations. Medication inserts should be carefully reviewed by the clinician for the equivalent high daily dosage.

Please refer to a separate policy on Site of Care or Site of Service Review (policy #2018030) for pharmacologic/biologic medications.

Does Not Meet Primary Coverage Criteria Or Is Investigational For Contracts Without Primary Coverage Criteria

Mepolizumab, for any indication or circumstance not described above, including but not limited to the below listed indications, does not meet member benefit certificate primary coverage criteria that there be scientific evidence of effectiveness in improving health outcomes.

1. Aspirin-exacerbated respiratory disease (AERD) or NSAID-exacerbated respiratory disease (NERD)- consists of 3 clinical features: asthma, nasal polyps, and sensitivity to aspirin and other NSAIDs.
2. Atopic dermatitis
3. Eosinophilic esophagitis

For members with contracts without primary coverage criteria, mepolizumab, for any indication or circumstance not described above, including but not limited to the below listed indications, is considered **investigational**.

1. Aspirin-exacerbated respiratory disease (AERD)
2. Atopic dermatitis
3. Eosinophilic esophagitis

Investigational services are specific contract exclusions in most member benefit certificates of coverage.