

# Pharmacy Policy Bulletin

**Title:** Interleukin-5 (IL-5) Antibody Agents

**Policy #:** Rx.01.223

**Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.**

**This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.**

**Members are advised to use participating pharmacies in order to receive the highest level of benefits.**

## **Intent:**

The intent of this policy is to communicate the medical necessity criteria for **mepolizumab (Nucala®) and benralizumab (Fasenra®)** as provided under the member's prescription drug benefit.

## **Description:**

Eosinophilic granulomatosis with polyangiitis (EGPA) is a multisystem disorder characterized by chronic rhinosinusitis, asthma, and prominent peripheral blood eosinophilia. The most commonly involved organ is the lungs, followed by the skin. EGPA can affect any organ system, including the cardiovascular, gastrointestinal, renal, and central nervous system. Vasculitis of extrapulmonary organs is largely responsible for the morbidity and mortality associated with EGPA.

The classification of "severe asthma" refers to patients who require high dose inhaled glucocorticoid (GC), or continuous or near continuous oral GC treatment to maintain asthma control or who never achieve control despite that treatment.

The National Asthma Education and Prevention Program (NAEPP) and Global Initiative for Asthma (GINA) guidelines have a slightly different category of "severe persistent asthma" that describes patients who have frequent and severe asthma symptoms and evidence of airflow limitation but are not on asthma controller medication. Patients with severe asthma (by European Respiratory Society [ERS]/American Thoracic Society [ATS] criteria) generally require high doses of controller medications to achieve control [1]; without these medications their asthma is either "not well controlled" or "very poorly controlled" by NAEPP/GINA criteria.

Some patients have persistently uncontrolled asthma despite high dose inhaled glucocorticoids and one or more nonglucocorticoid controller medications. Some of these patients may be candidates for anti-immunoglobulin E (anti-IgE) therapy, anti-interleukin-5 (anti-IL-5), or anti-IL-4 therapy, depending on factors such as their age, serum IgE level, and eosinophilic phenotype.

The biologic agents for severe asthma have not been compared in head-to-head trials, but certain patient and medication features help to guide selection. Only patients with an elevated eosinophil count are candidates for mepolizumab and other anti-interleukin (IL) agents; some agents are not approved for use under a certain age; and some agents require more or less frequent dosing.

The hypereosinophilic syndromes (HES) are a group of rare disorders marked by the sustained overproduction of eosinophils, in which eosinophilic infiltration and mediator release cause damage to multiple organs. The urgency of treatment and choice of therapy is based on the patient's presentation, as well as laboratory findings and the results of mutational analysis.

Mepolizumab (Nucala®) is an interleukin-5 (IL-5) antagonist monoclonal antibody that is subcutaneously administered for the treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA) or as an add-on maintenance treatment of adults and children 6 years of age or older with severe asthma of an eosinophilic phenotype, add-on maintenance treatment of adult patients 18 years and older with chronic rhinosinusitis with nasal polyps (CRSwNP), and 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. Nucala® autoinjector and prefilled syringe are commercially available for self-administration.

The exact mechanism of action of benralizumab (Fasenra®) in asthma has not been established, multiple cell types (mast cells, eosinophils, neutrophils, macrophages, lymphocytes) and mediators (histamine, eicosanoids, leukotrienes, cytokines)

are involved in inflammation. Benralizumab is a monoclonal antibody (IgG1, kappa) that causes apoptosis of eosinophils and basophils through antibody-dependent cell-mediated cytotoxicity.

Benralizumab (Fasenra®) is indicated for an add-on maintenance treatment of severe asthma in adults and children 12 years or older with an eosinophilic phenotype.

**Policy:**

**Severe Asthma**

**INITIAL CRITERIA:** Mepolizumab (Nucala®) is approved when ALL of the following are met:

1. Submission of documentation (e.g., chart notes, lab values) confirming diagnosis of severe asthma with eosinophilic phenotype as defined by ONE of the following:
  - a. Blood eosinophil levels are at least 150 cells/microliter at initiation of therapy (measured within 6 weeks of dosing); or
  - b. Blood eosinophil levels at least 300 cells/microliter within the past 12 months; and
2. Member is 6 years of age or older; and
3. One of the following:
  - a. Member has had at least two or more asthma exacerbations requiring systemic corticosteroids within the past 12 months; or
  - b. Prior asthma-related hospitalization within the past 12 months; and
4. Prescribed by or in consultation with pulmonologist or allergy/immunology specialist; and
5. Paid claims or submission of documentation (e.g., chart notes) confirming that the member is currently treated with high-dose inhaled corticosteroids (ICS) (e.g., greater than or equal to 500 mcg fluticasone propionate equivalent/day) and an additional controller medication (e.g., long-acting beta agonist such as salmeterol or formoterol, leukotriene inhibitor such as montelukast, theophylline), unless the individual is intolerant of or has a contraindication to two of the additional controller agents; and
6. No concurrent therapy with any other biologic agents; and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

**INITIAL CRITERIA:** Benralizumab (Fasenra®) is approved when ALL of the following are met:

1. Submission of documentation (e.g., chart notes, lab values) confirming diagnosis of severe asthma with eosinophilic phenotype as defined by ONE of the following:
  - a. Blood eosinophil levels are at least 150 cells/microliter at initiation of therapy (measured within 6 weeks of dosing); or
  - b. Blood eosinophil levels at least 300 cells/microliter within the past 12 months; and
2. One of the following:
  - a. Member has had at least two or more asthma exacerbations requiring systemic corticosteroids within the past 12 months; or
  - b. Prior asthma-related hospitalization within the past 12 months; and
3. Paid claims or submission of documentation (e.g., chart notes) confirming that the member is currently being treated or has a contraindication or intolerance to ONE of the following:
  - a. Both of the following:
    - i. High dose inhaled corticosteroids (ICS) [e.g., greater than 500 mcg fluticasone propionate equivalents/day]; and
    - ii. Additional asthma controller medication [e.g., leukotriene receptor antagonist, long-acting beta 2 agonist (LABA), theophylline]; or
  - b. One maximally dosed combination ICS/LABA product (e.g., Advair® [fluticasone propionate/salmeterol], Dulera® [mometasone/formoterol], Symbicort® [budesonide/formoterol]); and
4. Member is 12 years of age or older; and
5. Prescribed by or in consultation with pulmonologist or allergist/immunologist; and
6. No concurrent therapy with any other biologic agents; and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 2 years

**REAUTHORIZATION CRITERIA:** Mepolizumab (Nucala®) or Benralizumab (Fasenra®) is re-approved when ALL of the following are met:

1. Submission of documentation (e.g., chart notes) confirming a positive clinical response (e.g., reduction in exacerbations, improvement in forced expiratory volume in 1 second [FEV<sub>1</sub>], decreased use of rescue medications); and
2. Paid claims or submission of documentation (e.g., chart notes) confirming the member is currently being treated or has a contraindication or intolerance to ONE of the following:
  - a. Both of the following:
    - i. High dose inhaled corticosteroids (ICS) [e.g., greater than 500mcg fluticasone propionate equivalents/day]; and

- ii. Additional asthma controller medication [e.g., leukotriene receptor antagonist, long-acting beta 2 agonist (LABA), theophylline]; or
- b. One maximally dosed combination ICS/LABA product (e.g., Advair® [fluticasone propionate/salmeterol], Dulera® [mometasone/formoterol], Symbicort® (budesonide/formoterol)); and
- 3. Prescribed by or in consultation with pulmonologist or allergist/immunologist; and
- 4. No concurrent therapy with any other biologic agents; and
- 5. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Reauthorization duration: 2 years

<b>Mepolizumab (Nucala®)</b>	<b>DOSE</b>
Adults and pediatric patients aged 12 and older	100 mg every 4 weeks
Pediatric patients aged 6 to 11 years	40 mg every 4 weeks
<b>Benralizumab (Fasenra®)</b>	<b>DOSE</b>
Adults and pediatric patients aged 12 and older	Initial: 30 mg every 4 weeks for the first 3 doses Maintenance: 30 mg every 8 weeks

***Eosinophilic Granulomatosis with Polyangiitis (EGPA)***

**INITIAL CRITERIA:** Mepolizumab (Nucala®) is approved when ALL of the following are met:

- 1. Submission of documentation (e.g., chart notes) confirming a diagnosis of Eosinophilic Granulomatosis with Polyangiitis (EGPA); and
- 2. Paid claims or submission of medical records (e.g., chart notes) confirming that member's disease has relapsed or is refractory to standard of care therapy (i.e., prednisolone, prednisone); and
- 3. Patient is currently receiving corticosteroid therapy (e.g., prednisolone, prednisone); and
- 4. Member is 18 or older; and
- 5. Prescribed by or in consultation with pulmonologist, rheumatologist or allergy/immunology specialist; and
- 6. No concurrent therapy with any other biologic agents; and
- 7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial Authorization Duration: 2 years

**REAUTHORIZATION CRITERIA:** Mepolizumab (Nucala®) is re-approved when ALL of the following are met:

- 1. Submission of documentation (e.g., chart notes) confirming a positive clinical response to therapy (e.g., increase in remission time); and
- 2. Prescribed by or in consultation with a pulmonologist, rheumatologist or allergy/immunology specialist; and
- 3. No concurrent therapy with any other biologic agents; and
- 4. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Reauthorization duration: 2 years

<b>Mepolizumab (Nucala®)</b>	<b>DOSE</b>
Adults	300 mg as 3 separate 100-mg injections once every 4 weeks

***Hypereosinophilic Syndrome (HES)***

**INITIAL CRITERIA:** Mepolizumab (Nucala®) is approved when ALL of the following are met:

- 1. Submission of documentation (e.g., chart notes) confirming diagnosis of Hypereosinophilic Syndrome (HES); and
- 2. All of the following:
  - a. Member has been diagnosed for at least 6 months; and
  - b. Verification that other non-hematologic secondary causes have been ruled out (e.g., drug hypersensitivity, parasitic helminth infection, HIV infection, non-hematologic malignancy); and
  - c. Submission of documentation (e.g., chart notes, lab value) confirming that the member is FIP1-like-1-platelet derived growth factor receptor alpha kinase (FIP1L1-PDGFRα kinase)-negative

3. Member is 12 years old or older; and
4. Submission of documentation (e.g., chart notes, lab values) confirming member has uncontrolled HES defined by both of the following:
  - a. Pre-treatment blood eosinophil count greater than or equal to 1000 cells/microliter; and
  - b. Member has experienced 2 or more flares within the past 12 months; and
5. Paid claims or submission of documentation (e.g., chart notes) confirming inadequate response or inability to tolerate ONE of the following:
  - a. Corticosteroid therapy (e.g., prednisone); or
  - b. Cytotoxic/immunosuppressive therapy (e.g., hydroxyurea, cyclosporine, imatinib); and
6. Prescribed by or in consultation with one of the following:
  - a. Allergist/Immunologist; or
  - b. Hematologist; and
7. No concurrent therapy with any other biologic agents; and
8. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 2 years

**REAUTHORIZATION CRITERIA:** Mepolizumab (Nucala®) is re-approved when ALL of the following are met:

1. Submission of documentation of positive clinical response (e.g., reduction in corticosteroid use, reduction of blood eosinophil count, reduction in flares); and
2. Prescribed by or in consultation with one of the following:
  - a. Allergist/Immunologist; or
  - b. Hematologist; and
3. No concurrent therapy with any other biologic agents; and
4. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Reauthorization duration: 2 years

Mepolizumab (Nucala®)	DOSE
Adults and pediatric patients aged 12 and older	300 mg as 3 separate 100-mg injections once every 4 weeks

***Chronic rhinosinusitis with nasal polyps (CRSwNP)***

**INITIAL CRITERIA:** Mepolizumab (Nucala®) is approved when ALL of the following are met:

1. Submission of medical records (e.g., chart notes) confirming a diagnosis of chronic rhinosinusitis with nasal polyps (CRSwNP); and
2. Member is 18 years of age or older; and
3. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate at least a 2-month treatment with intranasal corticosteroids (e.g., fluticasone); and
4. Used in combination with another agent for CRSwNP; and
5. Prescribed by or in consultation with an allergist, immunologist, or Ear Nose Throat specialist; and
6. No concurrent therapy with any other biologic agents; and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 2 years

**REAUTHORIZATION CRITERIA:** Mepolizumab (Nucala®) is re-approved when ALL of the following are met:

1. Submission of medical records (e.g., chart notes) confirming documentation of positive clinical response to therapy (e.g., reduction in nasal polyps score [NPS: 0-8 scale], improvement in nasal obstruction symptoms via visual analog scale [VAS: 0-10 scale]); and
2. Used in combination with another agent for CRSwNP; and
3. Prescribed by or in consultation with an allergist, immunologist, or Ear Nose Throat specialist; and
4. No concurrent therapy with any other biologic agents; and
5. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Reauthorization duration: 2 years

Mepolizumab (Nucala®)	DOSE
Adults	100 mg every 4 weeks

**Black Box Warning as shown in the drug Prescribing Information:**

None

**Guidelines:**

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

**BENEFIT APPLICATION**

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

**References:**

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**Applicable Drugs:**

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

Mepolizumab (Nucala®)

Benralizumab (Fasenra®)

**Cross References:**

Off-Label Use Rx.01.33

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<b>Policy Version Number:</b>	10.00
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The Policy Bulletins on this web site were developed to assist the Company in administering the provisions of the respective benefit programs, and do not constitute a contract. If you have coverage through the Company, please refer to your specific benefit program for the terms, conditions, limitations and exclusions of your coverage. Company does not provide health care services, medical advice or treatment, or guarantee the outcome or results of any medical services/treatments. The facility and professional providers are responsible for providing medical advice and treatment. Facility and professional providers are independent contractors and are not employees or agents of the Company. If you have a specific medical condition, please consult with your doctor. The Company reserves the right at any time to change or update its Policy Bulletins.