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Section:	Prescription Drugs	**Effective Date:**	January 1, 2024
Subsection:	Respiratory Agents	**Original Policy Date:**	December 2, 2015
Subject:	IL-5 Antagonists (IgG1 kappa)	**Page:**	1 of 9

Last Review Date: December 8, 2023

IL-5 Antagonists (IgG1 kappa)

Description

Fasenra (benralizumab), Nucala (mepolizumab)

Background
Fasenra (benralizumab) and Nucala (mepolizumab) are used in combination with other asthma medications for the maintenance treatment of asthma in patients with an eosinophilic phenotype. Fasenra and Nucala are approved for patients who have a history of severe asthma attacks (exacerbations) despite receiving their current asthma medicines. Fasenra and Nucala reduce severe asthma attacks by reducing the levels of blood eosinophils, a type of white blood cell that contributes to the development of asthma. Nucala is also used in the treatment of certain eosinophilic conditions and in chronic rhinosinusitis with nasal polyps (CRSwNP) (1-2).

Regulatory Status
FDA-approved indications:

Fasenra is interleukin-5 receptor alpha-directed cytolytic monoclonal antibody (IgG1, kappa) indicated for add-on maintenance treatment of patients with severe asthma ages 12 years and older, and with an eosinophilic phenotype (2).

Nucala is an interleukin-5 antagonist monoclonal antibody (IgG1 kappa) indicated for: (1)

1. Add-on maintenance treatment of patients with severe asthma aged 6 years and older, and with an eosinophilic phenotype

2. Add-on maintenance treatment of adult patients 18 years and older with chronic rhinosinusitis with nasal polyps (CRSwNP) with inadequate response to nasal corticosteroids
3. The treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA)
4. 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

Limitations of Use: (1-2)

- Fasenra is not indicated for treatment of other eosinophilic conditions
- Fasenra and Nucala are not indicated for the relief of acute bronchospasm or status asthmaticus

Subjects enrolled in Nucala trial for severe asthma were required to have at least 1 of the following criteria: blood eosinophil count greater than or equal to 300 cells/mcL in past 12 months, eosinophil count greater than or equal 150 cells/mcL in the past 90 days or sputum eosinophil count greater than or equal to 3% (1).

In clinical trials herpes zoster have occurred in some patients receiving Fasenra or Nucala and varicella vaccination should be considered if medically appropriate prior to starting therapy (1-2).

Eosinophilic granulomatosis with polyangiitis (EGPA), which was previously called the Churg-Strauss syndrome (CSS) or allergic granulomatosis and angiitis, is a multisystem disorder characterized by allergic rhinitis, asthma, and prominent peripheral blood eosinophilia. Peripheral blood eosinophilia (usually 5000 to 9000 eosinophils/mcL) is the most characteristic finding, although levels over 1500 cells/mcL (or greater than 10 percent of the total leukocyte count) should prompt suspicion for EGPA. The primary therapy EGPA is systemic glucocorticoids. An additional immunosuppressive agent is typically added in patients with more advanced or refractory disease (3).

FEP adherence is defined as ≥ 50% utilization within the last 180 days.

Subjects enrolled in Nucala trial for HES had experienced at least 2 HES flares within the past 12 months and a blood eosinophil count of 1,000 cells/mcL or higher during screening. Patients must have been on stable HES therapy for the 4 weeks prior to randomization (1).

The safety and efficacy of Fasenra in pediatric patients less than 12 years of age have not been established (2).

The safety and efficacy of Nucala in pediatric patients less than 18 years of age with EGPA have not been established. The safety and efficacy of Nucala in pediatric patients less than 12 years of age with HES have not been established. The safety and efficacy of Nucala in pediatric patients less than 6 years of age with severe asthma have not been established (1).

Related policies
Cinqair, Dupixent, Tezspire, Xolair

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Fasenra and **Nucala** may be considered **medically necessary** if the conditions indicated below are met.

Fasenra and **Nucala** may be considered **investigational** for all other indications.

Prior-Approval Requirements

Diagnoses

Patient must have **ONE** of the following **AND** submission of medical records (e.g., chart notes, laboratory values) documenting the following:

Fasenra and Nucala

1. Severe asthma with an eosinophilic phenotype
    a. **Fasenra only:** 12 years of age or older
    b. **Nucala only:** 6 years of age or older
        i. **Age 6-11 only:** Prescriber will be dosing the patient within the FDA labeled maintenance dose of 40 mg subcutaneously every 4 weeks
    c. Inadequate control of asthma symptoms after a minimum of 3 months of compliant use with greater than or equal to 50% adherence with **ONE** of the following within the past 6 months:
        i. Inhaled corticosteroids & long acting $beta_2$ agonist
        ii. Inhaled corticosteroids & long acting muscarinic antagonist

d. Patient has **ONE** of the following:
    i. Eosinophil count greater than or equal 150 cells/mcL in the past 90 days
    ii. Eosinophil count greater than or equal 300 cells/mcL in the past 12 months
e. **NOT** used for the relief of acute bronchospasm or status asthmaticus

Nucala only

1. Chronic rhinosinusitis with nasal polyps (CRSwNP)
    a. 18 years of age or older
    b. Inadequate treatment response, intolerance, or contraindication to a 3-month trial of **TWO** nasal corticosteroid sprays (e.g., mometasone, fluticasone, budesonide, or triamcinolone)
    c. Used as add-on maintenance treatment
2. Eosinophilic granulomatosis with polyangiitis (EGPA)
    a. 18 years of age or older
    b. Inadequate treatment response, intolerance, or contraindication to **TWO** of the following medications:
        i. Systemic glucocorticoids
        ii. Cyclophosphamide
        iii. Azathioprine
        iv. Methotrexate
        v. Leflunomide
    c. Patient has **ONE** of the following:
        i. Eosinophil count greater than 1000 cells/mcL
        ii. Eosinophil count greater than 10% of the total leukocyte count
3. Hypereosinophilic syndrome (HES)
    a. 12 years of age or older
    b. Patient has had HES for at least 6 months
    c. **NO** identifiable non-hematologic secondary cause (e.g., drug hypersensitivity, parasitic helminth infection, HIV infection, non-hematologic malignancy)
    d. Patient has had HES flares while on stable HES therapy (such as chronic or episodic oral corticosteroids, immunosuppressive, or cytotoxic therapy)
    e. Eosinophil count greater than or equal to 1000 cells/mcL

AND ALL of the following for **ALL** indications:

1. **NO** dual therapy with another monoclonal antibody for the treatment of the requested indication
2. Prescriber will assess the medical appropriateness for a varicella vaccination prior to therapy

All approved requests are subject to review by a clinical specialist for final validation and coverage determination once all required documentation has been received. Current utilization, including samples, does not guarantee approval of coverage.

Prior – Approval *Renewal* Requirements

Diagnoses

Patient must have **ONE** of the following **AND** submission of medical records (e.g., chart notes, laboratory values) documenting the following:

Fasenra and Nucala

1. Asthma with an eosinophilic phenotype
    a. **Fasenra only:** 12 years of age or older
    b. **Nucala only:** 6 years of age or older
        i. **Age 6-11 only:** Prescriber will be dosing the patient within the FDA labeled maintenance dose of 40 mg subcutaneously every 4 weeks
    c. Decreased exacerbations **OR** improvement in symptoms
    d. Decreased utilization of rescue medications
    e. Patient has been compliant on Fasenra/Nucala therapy
    f. **NOT** used for the relief of acute bronchospasm or status asthmaticus

Nucala only

1. Chronic rhinosinusitis with nasal polyps (CRSwNP)
    a. 18 years of age or older
    b. Improvement in sino-nasal symptoms
    c. Used as add-on maintenance treatment
2. Eosinophilic granulomatosis with polyangiitis (EGPA)
    a. 18 years of age or older
    b. Improvement in symptoms
3. Hypereosinophilic syndrome (HES)
    a. 12 years or age or older

b. Improvement in symptoms and/or reduction in the number of flares

AND the following for **ALL** indications:

1. **NO** dual therapy with another monoclonal antibody for the treatment of the requested indication

All approved requests are subject to review by a clinical specialist for final validation and coverage determination once all required documentation has been received. Current utilization, including samples, does not guarantee approval of coverage.

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity

Age (years)	Indication	Drug/Strength	Quantity
12+	Asthma	Fasenra 30 mg	5 syringes/pens per 180 days **OR**
6-11	Asthma	Nucala 40 mg Nucala 100 mg vial	3 injections per 84 days **OR**
12+	Asthma	Nucala 100 mg	3 injections per 84 days **OR**
18+	CRSwNP	Nucala 100 mg	3 injections per 84 days **OR**
18+	EGPA	Nucala 100 mg	9 injections per 84 days **OR**
12+	HES	Nucala 100 mg	9 injections per 84 days

Duration 6 months

Prior – Approval *Renewal* Limits

Quantity

Age (years)	Indication	Drug/Strength	Quantity
12+	Asthma	Fasenra 30 mg	3 syringes/pens per 168 days **OR**
6-11	Asthma	Nucala 40 mg	3 injections per 84 days **OR**

		Nucala 100 mg vial	
12+	Asthma	Nucala 100 mg	3 injections per 84 days **OR**
18+	CRSwNP	Nucala 100 mg	3 injections per 84 days **OR**
18+	EGPA	Nucala 100 mg	9 injections per 84 days **OR**
12+	HES	Nucala 100 mg	9 injections per 84 days

Duration 12 months

Rationale

Summary

Fasenra (benralizumab) and Nucala (mepolizumab) are used in combination with other asthma medications for the maintenance treatment of asthma in patients with an eosinophilic phenotype. Fasenra and Nucala have been shown to decrease the incidence of asthma exacerbations in patients with severe asthma whose symptoms are inadequately controlled with inhaled corticosteroids. Nucala is also used in the treatment of certain eosinophilic conditions and in chronic rhinosinusitis with nasal polyps (CRSwNP). Fasenra and Nucala are not indicated for the relief of acute bronchospasm or status asthmaticus (1-2).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Fasenra and Nucala while maintaining optimal therapeutic outcomes.

References

1. Nucala [package insert]. Philadelphia, PA: GlaxoSmithKline LLC; March 2023.
2. Fasenra [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; February 2021.
3. Gioffredi A, Maritati F, et al. Eosinophilic Granulomatosis with Polyangiitis: An Overview. Front Immunol. 2014; 5: 549.
4. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2019. Available from www.ginasthma.org.

Policy History

Date	Action
December 2015	Addition to PA
March 2016	Annual editorial review Addition of the requirement of the patient must have one of the following: eosinophil count greater than or equal 150 cells/ mcL in the past 90 days, or

	eosinophil count greater than or equal 300 cells/mcL in the past 12 months also, varicella vaccination has been given prior to Nucala therapy per SME Policy number change from 5.13.07
June 2016	Annual review
September 2016	Clarified dual therapy statement and addition of age to renewal Change of the varicella vaccination requirement to Prescriber will assess the medical appropriateness for a varicella vaccination prior to therapy
March 2017	Annual editorial review
December 2017	Addition of Fasenra and quantity limits on both medications
January 2018	Addition of new indication for Nucala eosinophilic granulomatosis with polyangiitis (EGPA). Removal of the requirement for other eosinophilic conditions
March 2018	Annual review
June 2018	Annual editorial review Addition of requirement for asthma: Inadequate control of asthmatic symptoms after a minimum of 3 months of ONE of the following: Inhaled corticosteroids & long acting beta$_2$ agonist or Inhaled corticosteroids & long acting muscarinic antagonist
November 2018	Change of Nucala eosinophil count requirement from > 1500 cells/mcL to > 1000 cells/mcL
March 2019	Annual review
August 2019	Addition of the 50% adherence requirement to the asthma diagnosis. Removed requirement to use in combination with ICS + LABA and addition of renewal requirement to be compliant on therapy. Addition to managed PA program
September 2019	Annual review and reference update. Decreased Nucala age limit for severe asthma to 6 and older from 12 and older and added requirement to dose within FDA labeled maintenance dose for patients age 6-11 for Nucala
March 2020	Annual review and reference update
October 2020	Addition of indication for Nucala: hypereosinophilic syndrome (HES)
December 2020	Annual review
May 2021	Reference update
June 2021	Annual review
August 2021	Addition of indication for Nucala: chronic rhinosinusitis with nasal polyps (CRSwNP)
September 2021	Annual review
January 2022	Revised no dual therapy requirement to “no dual therapy with another monoclonal antibody for the treatment of the requested indication”
March 2022	Annual editorial review and reference update. Added new dosage form Nucala 40mg for patients age 6-11 years old with severe asthma. Nucala day supply changed from 90 to 84 to reflect once every 4 weeks dosing. Fasenra renewal day supply changed from 180 to 168 to reflect once every

	8 weeks dosing. Moved the requirement “NOT used for the relief of acute bronchospasm or status asthmaticus” under the asthma indication
June 2022	Annual review
September 2022	Annual review
June 2023	Annual review and reference update
December 2023	Annual review. Per SME, changed renewal requirement to decreased exacerbations or improvement in symptoms. Also revised Fasenra mechanism of action

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 8, 2023 and is effective on January 1, 2024.