

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Immunologicals – Nucala Utilization Management Medical Policy

- Nucala® (mepolizumab subcutaneous injection – GlaxoSmithKline)

REVIEW DATE: 06/04/2025; selected revision 11/05/2025

OVERVIEW

Nucala, an interleukin (IL)-5 antagonist monoclonal antibody, is indicated for the following uses:¹

- **Asthma**, as add-on maintenance treatment of patients \geq 6 years of age with severe disease with an eosinophilic phenotype. Limitations of Use: Nucala is not indicated for the relief of acute bronchospasm or status asthmaticus.
- **Chronic obstructive pulmonary disease (COPD)**, as add-on maintenance treatment in patients \geq 18 years of age with inadequately controlled disease and an eosinophilic phenotype.
Limitation of Use: Nucala is not indicated for the relief of acute bronchospasm.
- **Chronic rhinosinusitis with nasal polyps (CRSwNP)**, as an add-on maintenance treatment in patients \geq 18 years of age with an inadequate response to nasal corticosteroids.
- **Eosinophilic granulomatosis with polyangiitis (EGPA)** [formerly known as Churg-Strauss Syndrome] in adult patients.
- **Hypereosinophilic syndrome (HES)**, in patients \geq 12 years of age who have had HES for \geq 6 months without an identifiable non-hematologic secondary cause.

Clinical Efficacy

Asthma

In the pivotal asthma studies of Nucala, patients were generally required to have elevated eosinophils at baseline (e.g., peripheral blood eosinophil count \geq 150 cells/microliter at screening or \geq 300 cells/microliter at some time during the previous year). Across the studies, efficacy was assessed as early as 24 weeks.¹⁻⁴

Chronic Obstructive Pulmonary Disease

Data to support the use of Nucala in COPD come from one pivotal study, MATINEE, and a subgroup of patients with elevated eosinophils in a second pivotal study, METREX.^{22,23} To be eligible for enrollment in MATINEE, patients had a blood eosinophil level \geq 300 cells per microliter at screening and a level \geq 150 cells per microliter within 12 months of study enrollment. Patients were required to have been receiving background triple inhaler therapy (i.e., an inhaled corticosteroid [ICS] with a long-acting muscarinic antagonist [LAMA] and a long-acting beta₂-agonist [LABA]), for at least 3 months prior to randomization. Patients also experienced at least two moderate COPD exacerbations requiring treatment with a systemic corticosteroid with or without antibiotics, or at least one severe COPD exacerbation requiring hospitalization for \geq 24 hours during the year prior to screening. Patients were randomized to receive either Nucala or placebo in addition to background maintenance therapy for 52 weeks (METREX) or 52 to 104 weeks (MATINEE).

Chronic Rhinosinusitis with Nasal Polyps

In one pivotal study involving adult patients with chronic rhinosinusitis with nasal polyposis, the primary efficacy endpoints were assessed at 52 weeks.^{1,5} However, improvements in nasal polyp size and symptoms compared with placebo were observed much earlier on in the course of treatment (i.e., between 9 and 24 weeks). Patients were required to be symptomatic prior to study enrollment.

Eosinophilic Granulomatosis with Polyangiitis

One study evaluated the efficacy of Nucala in patients ≥ 18 years of age with relapsing or refractory EGPA who had received ≥ 4 weeks of a stable oral corticosteroid dose (i.e., prednisolone, prednisone).⁶ Patients were also required to have a baseline relative eosinophil level of 10% or an absolute eosinophil level $> 1,000$ cells per microliter; however, the baseline mean absolute eosinophil level was approximately 175 cells per microliter across both treatment groups. While remission benefit of Nucala was demonstrated in the overall patient population, the magnitude of improvements observed with Nucala were larger in patients with baseline eosinophil levels ≥ 150 cells per microliter than in patients with lower baseline levels. An additional study evaluated the efficacy of Nucala compared with another anti-IL-5 agent, Fasenra[®] (benralizumab subcutaneous injection), in patients ≥ 18 years of age with relapsing or refractory EGPA who had received ≥ 4 weeks of a stable oral corticosteroid dose (i.e., prednisolone, prednisone, methylprednisolone, or hydrocortisone).³⁰ The primary endpoint was the proportion of patients in remission at both Week 36 and Week 48.

Hypereosinophilic Syndrome

One study evaluated the efficacy of Nucala in patients ≥ 12 years of age with hypereosinophilic syndrome for ≥ 6 months.⁷ Patients with non-hematologic secondary hypereosinophilic syndrome and those with FIP1L1-PDGFR α kinase-positive hypereosinophilic syndrome were excluded. All patients had a baseline blood eosinophil count $\geq 1,000$ cells per microliter. Additionally, all patients had been on stable therapy for their hypereosinophilic syndrome (e.g., oral corticosteroids, immunosuppressive agents, or cytotoxic therapy) for 4 weeks or more prior to randomization. Efficacy was assessed following 32 weeks of therapy.

Guidelines

Asthma Guidelines

The Global Initiative for Asthma Global Strategy for Asthma Management and Prevention (2025) proposes a step-wise approach to asthma treatment.⁸ Nucala is listed as an option for add-on therapy in patients ≥ 6 years of age with severe eosinophilic asthma. Severe asthma is defined as asthma that is uncontrolled despite adherence to optimized high-dose inhaled corticosteroid (ICS)/long-acting beta₂-agonist (LABA) therapy or that worsens when high-dose treatment is decreased. Higher blood eosinophil levels, higher number of severe exacerbations in the previous year, adult-onset asthma, nasal polyps, maintenance oral corticosteroid requirements, and low lung function may predict a good asthma response to Nucala.

According to the European Respiratory Society/American Thoracic Society guidelines (2014; updated in 2020), severe asthma is defined as asthma which requires treatment with a high-dose ICS in addition to a second controller medication (and/or systemic corticosteroids) to prevent it from becoming uncontrolled, or asthma which remains uncontrolled despite this therapy.^{9,10} Uncontrolled asthma is defined as asthma that worsens upon tapering of high-dose ICS or systemic corticosteroids or asthma that meets one of the following four criteria:

- 1) Poor symptom control: Asthma Control Questionnaire consistently ≥ 1.5 or Asthma Control Test < 20 ;
- 2) Frequent severe exacerbations: two or more bursts of systemic corticosteroids in the previous year;
- 3) Serious exacerbations: at least one hospitalization, intensive care unit stay, or mechanical ventilation in the previous year;
- 4) Airflow limitation: forced expiratory volume in 1 second (FEV₁) $< 80\%$ predicted after appropriate bronchodilator withholding.

Chronic Obstructive Pulmonary Disease Guidelines

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease (2025) recommends triple inhaled therapy with an ICS/LAMA/LABA combination in patients with a history of exacerbations and elevated eosinophils.²⁴ However, guidelines note that ICS therapy increases the risk of pneumonia in patients with COPD, particularly those with severe disease. Nucala is not currently addressed in GOLD recommendations.

Chronic Rhinosinusitis with Nasal Polyps Guidelines

The Joint Task Force on Practice Parameters (JTFPP) published a focused guideline update for the medical management of CRSwNP (2023), which updated recommendations regarding intranasal corticosteroids and biologic therapies.¹¹ Intranasal corticosteroids are recommended for the treatment of CRSwNP. Use of biologics (e.g., Nucala) is also recommended. However, in patients who derived a sufficient benefit from other therapies such as intranasal corticosteroids, surgery, or aspirin therapy after desensitization, biologics may not be preferred. Conversely, biologics may be preferred over other medical treatment options in patients who continue to have a high burden of disease despite receiving at least 4 weeks of treatment with an intranasal corticosteroid.

The diagnosis of CRSwNP was not addressed in this focused guideline update. Previous guidelines have noted that the presence of two or more signs and symptoms of chronic rhinosinusitis (e.g., rhinorrhea, postnasal drainage, anosmia, nasal congestion, facial pain, headache, fever, cough, and purulent discharge) that persist for an extended period of time makes the diagnosis of chronic rhinosinusitis likely.¹²⁻¹⁵ However, this requires confirmation of sinonasal inflammation, which can either be done via direct visualization or computed tomography (CT) scan. Oral corticosteroids and surgical intervention were not specifically addressed in this update. Prior guidelines recommend short courses of oral corticosteroid as needed and consideration of surgical removal as an adjunct to medical therapy in patients with CRSwNP that is not responsive or is poorly responsive to medical therapy.^{12,13,15}

Eosinophilic Granulomatosis with Polyangiitis Guidelines

The American College of Rheumatology (ACR)/Vasculitis Foundation Guideline for the Management of Antineutrophil Cytoplasmic Antibody-Associated (ANCA) Vasculitis (2021) includes recommendations regarding the management of EGPA.¹⁶ For patients with active, non-severe EGPA, combination therapy with Nucala and corticosteroids is recommended over other traditional treatments such as methotrexate, azathioprine, or mycophenolate mofetil in the setting of remission induction. Non-severe EGPA is defined as vasculitis in the absence of life- or organ-threatening manifestations. In general, the clinical profile includes rhinosinusitis, asthma, mild systemic symptoms, uncomplicated cutaneous disease, and mild inflammatory arthritis. Nucala, in combination with corticosteroids, is also a recommended therapy for patients who have relapsed and are experiencing non-severe disease manifestations (i.e., asthma and/or sinonasal disease) while receiving either low-dose corticosteroids alone, methotrexate, azathioprine, or mycophenolate mofetil. For patients with severe EGPA, cyclophosphamide or rituximab is preferred over Nucala for remission induction. The European Alliance of Associations for Rheumatology (EULAR) recommendations for the management of ANCA-associated vasculitis (2022) also address the use of Nucala for the treatment of EGPA.¹⁷ Similar to the ACR guidelines, EULAR recommends Nucala for induction of remission in patients with relapsing or refractory EGPA without active organ- or life-threatening disease. It is also recommended for maintenance of remission in these patients. Additionally, it is also among the many recommended treatment options for the maintenance of remission of EGPA after induction of remission for organ-threatening or life-threatening disease.

Hypereosinophilia Guidelines

The World Health Organization (WHO) and international consensus classification of eosinophilic disorders update on diagnosis, risk stratification, and management (2024) notes that corticosteroids remain first-line therapy for the treatment of HES.¹⁸ Nucala, hydroxyurea, pegylated-interferon, imatinib, and hematopoietic stem cell transplantation are listed as second-line treatment options.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Nucala. Approval is recommended for those who meet the **Criteria and Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the durations noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Nucala, as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Nucala to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Nucala is recommended in those who meet one of the following criteria:

FDA-Approved Indications

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- 1) Asthma.** Approve Nucala for the duration noted if the patient meets ONE of the following (A or B):
- A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, iv, and v):
- i. Patient is \geq 6 years of age; AND
 - ii. Patient meets ONE of the following (a or b):
- a) Patient has a blood eosinophil level \geq 150 cells per microliter within the previous 6 weeks; OR
 - b) Patient had a blood eosinophil level \geq 150 cells per microliter prior to treatment with Nucala or another monoclonal antibody therapy that may alter blood eosinophil levels; AND
- Note: Examples of monoclonal antibody therapies that may alter blood eosinophil levels include Nucala, Adbry (tralokinumab-ldrm subcutaneous injection), Cinqair (reslizumab intravenous infusion), Dupixent (dupilumab subcutaneous injection), Ebglyss (lebrikizumab-lbkz subcutaneous injection), Fasenra (benralizumab subcutaneous injection), Nemluvio (nemolizumab-ilto subcutaneous injection), Tezspire (tezepelumab-ekko subcutaneous injection), Xolair (omalizumab subcutaneous injection).
- iii. Patient has received at least 3 consecutive months of combination therapy with BOTH of the following (a and b):
- a) An inhaled corticosteroid; AND
 - b) At least one additional asthma controller or asthma maintenance medication; AND
- Note: Examples of additional asthma controller or asthma maintenance medications are inhaled long-acting beta₂-agonists, inhaled long-acting muscarinic antagonists, and monoclonal antibody therapies for asthma (e.g., Cinqair, Dupixent, Fasenra, Nucala,

Tezspire, Xolair). Use of a combination inhaler containing both an inhaled corticosteroid and additional asthma controller/maintenance medication(s) would fulfill the requirement for both criteria a and b.

- iv. Patient has asthma that is uncontrolled or was uncontrolled at baseline as defined by ONE of the following (a, b, c, d, or e):

Note: “Baseline” is defined as prior to receiving Nucala or another monoclonal antibody therapy for asthma. Examples of monoclonal antibody therapies for asthma include Nucala, Cinqair, Dupixent, Fasenra, Tezspire, and Xolair.

- a) Patient experienced two or more asthma exacerbations requiring treatment with systemic corticosteroids in the previous year; OR
- b) Patient experienced one or more asthma exacerbation(s) requiring a hospitalization, an emergency department visit, or an urgent care visit in the previous year; OR
- c) Patient has a forced expiratory volume in 1 second (FEV₁) < 80% predicted; OR
- d) Patient has an FEV₁/forced vital capacity (FVC) < 0.80; OR
- e) Patient has asthma that worsens upon tapering of oral (systemic) corticosteroid therapy; AND

- v. The medication is prescribed by or in consultation with an allergist, immunologist, or pulmonologist; OR

- B) Patient is Currently Receiving Nucala. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):

- i. Patient has already received at least 6 months of therapy with Nucala; AND

Note: A patient who has received < 6 months of therapy or who is restarting therapy with Nucala should be considered under criterion 1A (Asthma, Initial Therapy).

- ii. Patient continues to receive therapy with one inhaled corticosteroid or one inhaled corticosteroid-containing combination inhaler; AND

- iii. Patient has responded to therapy as determined by the prescriber.

Note: Examples of a response to Nucala therapy are decreased asthma exacerbations; decreased asthma symptoms; decreased hospitalizations, emergency department, urgent care, or medical clinic visits due to asthma; and decreased requirement for oral corticosteroid therapy.

Dosing. Approve ONE of the following dosing regimens (A or B):

- A) If the patient is ≥ 12 years of age, approve 100 mg administered subcutaneously once every 4 weeks; OR

- B) If the patient is 6 to 11 years of age, approve 40 mg administered subcutaneously once every 4 weeks.

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2. **Chronic Obstructive Pulmonary Disease (COPD).** Approve for the duration noted if the patient meets ONE of the following (A or B):

- A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, iv, and v):

- i. Patient is ≥ 18 years of age; AND

- ii. Patient meets ONE of the following (a or b):

- a) Patient has a blood eosinophil level ≥ 300 cells per microliter within the previous 6 weeks; OR

- b) Patient had a blood eosinophil level ≥ 300 cells per microliter prior to treatment with Nucala or another monoclonal antibody therapy that may alter blood eosinophil levels; AND

Note: Examples of monoclonal antibody therapies that may alter blood eosinophil levels include Nucala, Adbry (tralokinumab-1drm subcutaneous injection), Cinqair (reslizumab intravenous infusion), Dupixent (dupilumab subcutaneous injection); Ebglyss (lebrikizumab-lbkz subcutaneous injection); Fasenra (benralizumab subcutaneous injection), Nemluvio (nemolizumab-ilto subcutaneous injection); Tezspire (tezepelumab subcutaneous injection), and Xolair (omalizumab subcutaneous injection).

iii. Patient meets ONE of the following (a or b):

- a) Patient has received at least 3 consecutive months of combination therapy with ALL of the following (1, 2, and 3):

- (1) Inhaled long-acting beta₂-agonist (LABA); AND
(2) Inhaled long-acting muscarinic antagonist (LAMA); AND
(3) Inhaled corticosteroid (ICS); OR

Note: Use of single-entity inhalers or a combination inhaler containing multiple agents from the medication classes listed would fulfill the requirement.

- b) Patient meets BOTH of the following (1 and 2):

- (1) Patient has received at least 3 consecutive months of combination therapy with an inhaled LABA and an inhaled LAMA; AND

Note: Use of single-entity inhalers or a combination inhaler containing multiple agents from the medication classes listed would fulfill the requirement.

- (2) According to the prescriber, the patient has a contraindication to the use of an inhaled corticosteroid; AND

iv. Patient meets ONE of the following (a or b):

- a) Patient experienced two or more COPD exacerbations requiring treatment with a systemic corticosteroid with or without an antibiotic in the previous 12 months; OR

- b) Patient experienced one or more COPD exacerbation(s) requiring a hospitalization in the previous 12 months; AND

Note: A hospitalization includes a hospital admission or an emergency medical care visit with observation lasting > 24 hours.

v. The medication is prescribed by or in consultation with an allergist, immunologist, or pulmonologist; OR

B) Patient is Currently Receiving Nucala. Approve for 1 year if the patient meets the following (i, ii, and iii):

i. Patient has already received at least 6 months of therapy with Nucala; AND

Note: A patient who has received < 6 months of therapy or who is restarting therapy with Nucala should be considered under criterion 2A (Chronic Obstructive Pulmonary Disease, Initial Therapy).

ii. Patient continues to receive combination therapy with an inhaled LABA and LAMA; AND

Note: Use of single-entity inhalers or a combination inhaler containing multiple agents from the medication classes listed would fulfill the requirement.

iii. Patient has experienced a beneficial clinical response, defined by ONE of the following (a, b, c, d, or e):

- a) Reduced COPD symptoms; OR

- b) Reduced COPD exacerbations; OR

- c) Reduced COPD-related hospitalizations; OR

- d) Reduced emergency department or urgent care visits; OR

- e) Improved lung function parameters.

Dosing. Approve 100 mg administered subcutaneously once every 4 weeks.

3) Chronic Rhinosinusitis with Nasal Polyps. Approve Nucala for the duration noted if the patient meets ONE of the following (A or B):

- A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, iv, v, vi and vii):
- i. Patient is \geq 18 years of age; AND
 - ii. Patient has chronic rhinosinusitis with nasal polyps as evidenced by direct examination, endoscopy, or sinus computed tomography (CT) scan; AND
 - iii. Patient has had the diagnosis of chronic rhinosinusitis with nasal polyps for at least 6 months; AND
 - iv. Patient has experienced two or more of the following symptoms for at least 8 weeks: nasal congestion, nasal obstruction, nasal discharge, and/or reduction/loss of smell; AND
 - v. Patient meets BOTH of the following (a and b):
 - a) Patient has received at least 4 weeks of therapy with an intranasal corticosteroid; AND
 - b) Patient will continue to receive therapy with an intranasal corticosteroid concomitantly with Nucala; AND
 - vi. Patient meets ONE of the following (a, b, or c):
 - a) Patient has received at least one course of treatment with a systemic corticosteroid within the previous year; OR
 - Note: One course of a systemic corticosteroid is \geq 3 consecutive days of treatment or one long-acting injectable dose.
 - b) Patient has a contraindication to systemic corticosteroid therapy; OR
 - c) Patient has had prior surgery for nasal polyps; AND
 - vii. Nucala is prescribed by or in consultation with an allergist, immunologist, or an otolaryngologist (ear, nose and throat [ENT] physician specialist); OR

B) Patient is Currently Receiving Nucala. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):

- i. Patient has already received at least 6 months of therapy with Nucala; AND
 - Note: A patient who has received $<$ 6 months of therapy or who is restarting therapy with Nucala should be considered under criterion 3A (Chronic Rhinosinusitis with Nasal Polyps, Initial Therapy).
- ii. Patient continues to receive therapy with an intranasal corticosteroid; AND
- iii. Patient has responded to therapy as determined by the prescriber.
 - Note: Examples of a response to Nucala therapy are reduced nasal polyp size, improved nasal congestion, reduced sinus opacification, decreased sino-nasal symptoms, improved sense of smell.

Dosing. Approve 100 mg administered subcutaneously once every 4 weeks.

4) Eosinophilic Granulomatosis with Polyangiitis (EGPA) [formerly known as Churg-Strauss Syndrome]. Approve Nucala for the duration noted if the patient meets ONE of the following (A or B):

- A) Initial Therapy. Approve for 9 months if the patient meets ALL of the following (i, ii, iii, and iv):
- i. Patient is \geq 18 years of age; AND
 - ii. Patient has active, non-severe disease; AND
 - Note: Non-severe disease is defined as vasculitis without life- or organ-threatening manifestations. Examples of symptoms in patients with non-severe disease include rhinosinusitis, asthma, mild systemic symptoms, uncomplicated cutaneous disease, mild inflammatory arthritis.
 - iii. Patient meets BOTH of the following (a and b):

- a)** Patient is currently receiving a systemic corticosteroid (e.g., prednisone) and has been on therapy for a minimum of 4 weeks; AND
 - b)** Patient meets ONE of the following [(1) or (2)]:
 - (1) Patient has a blood eosinophil level ≥ 150 cells per microliter within the previous 4 weeks; OR
 - (2) Patient had a blood eosinophil level ≥ 150 cells per microliter prior to treatment with Nucala or another monoclonal antibody therapy that may alter blood eosinophil levels; AND

Note: Examples of monoclonal antibody therapies that may alter blood eosinophil levels include Nucala, Adbry (tralokinumab-ldrm subcutaneous injection), Cinqair (reslizumab intravenous infusion), Dupixent (dupilumab subcutaneous injection), Ebglyss (lebrikizumab-lbkz subcutaneous injection), Fasenra (benralizumab subcutaneous injection), Nemluvio (nemolizumab-ilto subcutaneous injection), Tezspire (tezepelumab-ekko subcutaneous injection), Xolair (omalizumab subcutaneous injection).
 - iv. The medication is prescribed by or in consultation with an allergist, immunologist, pulmonologist, or rheumatologist; OR
- B)** Patient is Currently Receiving Nucala. Approve for 1 year if the patient meets BOTH of the following (i and ii):
- i. Patient has already received at least 9 months of therapy with Nucala; AND
 - Note: A patient who has received < 9 months of therapy or who is restarting therapy with Nucala should be considered under criterion 4A (Eosinophilic Granulomatosis with Polyangiitis, Initial Therapy).
 - ii. Patient has responded to therapy as determined by the prescriber.
 - Note: Examples of a response to Nucala therapy are reduced rate of relapse, corticosteroid dose reduction, and reduced eosinophil levels.

Dosing. Approve 300 mg administered subcutaneously once every 4 weeks.

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- 5) Hypereosinophilic Syndrome.** Approve Nucala for the duration noted if the patient meets ONE of the following (A or B):
- A)** Initial Therapy. Approve for 8 months if the patient meets ALL of the following (i, ii, iii, iv, v, vi, and vii):
- i. Patient is ≥ 12 years of age; AND
 - ii. Patient has had hypereosinophilic syndrome for ≥ 6 months; AND
 - iii. Patient has FIP1L1-PDGFR α -negative disease; AND
 - iv. Patient does NOT have an identifiable non-hematologic secondary cause of hypereosinophilic syndrome according to the prescriber; AND
 - Note: Examples of secondary causes of hypereosinophilic syndrome include drug hypersensitivity, parasitic helminth infection, human immunodeficiency virus infection, non-hematologic malignancy.
 - v. Patient has/had a blood eosinophil level $\geq 1,000$ cells per microliter prior to treatment with any monoclonal antibody therapy that may alter blood eosinophil levels; AND
 - Note: Examples of monoclonal antibody therapies that may alter blood eosinophil levels include Nucala, Adbry (tralokinumab-ldrm subcutaneous injection), Cinqair (reslizumab intravenous infusion), Dupixent (dupilumab subcutaneous injection), Ebglyss (lebrikizumab-lbkz subcutaneous injection), Fasenra (benralizumab subcutaneous injection), Nemluvio (nemolizumab-ilto subcutaneous injection), Tezspire (tezepelumab-ekko subcutaneous injection), Xolair (omalizumab subcutaneous injection).

- vi. Patient has tried at least one other treatment for hypereosinophilic syndrome for a minimum of 4 weeks; AND

Note: Example of treatments for hypereosinophilic syndrome include systemic corticosteroids, hydroxyurea, cyclosporine, imatinib, or pegylated-interferon.

- vii. Nucala is prescribed by or in consultation with an allergist, immunologist, pulmonologist, or rheumatologist; OR

- B) Patient is Currently Receiving Nucala.** Approve for 1 year if the patient meets BOTH of the following (i and ii):

- i. Patient has already received at least 8 months of therapy with Nucala; AND

Note: A patient who has received < 8 months of therapy or who is restarting therapy with Nucala should be considered under criterion 4A (Hypereosinophilic Syndrome, Initial Therapy).

- ii. Patient has responded to therapy as determined by the prescriber.

Note: Examples of a response to Nucala therapy are decreased number of flares, improved fatigue, reduced corticosteroid requirements, and decreased eosinophil levels.

Dosing. Approve 300 mg administered subcutaneously once every 4 weeks.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Nucala is not recommended in the following situations:

1. **Atopic Dermatitis.** Nucala is not indicated for the treatment of atopic dermatitis.¹ In one small study, intravenous (IV) mepolizumab significantly reduced peripheral blood eosinophil counts in patients with moderate to severe atopic dermatitis.^{19,20} However, mepolizumab IV therapy did not result in clinical success as assessed by Physician's Global Assessment of Improvement scores compared with placebo. Other clinical outcomes were also not significantly improved with mepolizumab IV. Another small study evaluated subcutaneous Nucala in patients with moderate to severe atopic dermatitis.²¹ Following 16 weeks of therapy, Nucala did not demonstrate efficacy, with 11% (n = 2/11) of patients meeting the primary endpoint of treatment success with Nucala vs. 0 with placebo. Further research is warranted to determine if Nucala has a place in therapy in the treatment of these conditions.

2. **Concurrent use of Nucala with another Monoclonal Antibody Therapy.** The efficacy and safety of Nucala used in combination with other monoclonal antibody therapies have not been established.
Note: Monoclonal antibody therapies are Adbry® (tralokinumab-ldrm subcutaneous injection), Cinqair® (reslizumab intravenous injection), Dupixent® (dupilumab subcutaneous injection), Ebglyss® (lebrikizumab-lbkz subcutaneous injection), Fasenra® (benralizumab subcutaneous injection), Nemluvio® (nemolizumab-ilto subcutaneous injection), Tezspire® (tezepelumab-ekko subcutaneous injection), or Xolair® (omalizumab subcutaneous injection).

3. **Eosinophilic Esophagitis (EoE), Eosinophilic Gastroenteritis, or Eosinophilic Colitis.** Nucala is not indicated for the treatment of eosinophilic esophagitis, eosinophilic gastroenteritis or eosinophilic colitis.¹ A few small studies reported IV mepolizumab to be efficacious in these conditions.²⁵⁻²⁷ Of note, Nucala is not approved for IV administration.¹ One randomized, double-blind trial (n = 66) evaluated the efficacy of Nucala in patients with EoE.²⁸ Following 3 months of therapy, there was no statistically significant improvement in dysphagia symptoms with Nucala vs. placebo, as measured by the EoE Symptom Activity Index (EEsAI) [primary endpoint]. The EEsAI was also not significantly different between the two treatment groups at 6 months of treatment. However, significantly more patients achieved a histologic response (i.e., < 15 eosinophils/high-power field) with Nucala compared with placebo. Clinical guidelines on the diagnosis and management of eosinophilic esophagitis from

the American College of Gastroenterology (2025) do not make a recommendation for or against Nucala citing inconsistent data.²⁹ Further research is warranted to determine if Nucala has a place in therapy in the treatment of these conditions.

4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Nucala® subcutaneous injection [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; March 2023.
2. Pavord ID, Korn S, Howarth P, et al. Mepolizumab for severe eosinophilic asthma (DREAM): a multicentre, double-blind, placebo-controlled trial. *Lancet*. 2012;380:651-659.
3. Ortega HG, Liu MC, Pavord ID, et al. Mepolizumab treatment in patients with severe eosinophilic asthma. *N Engl J Med*. 2014;371:1198-1207.
4. Bel EH, Wenzel SE, Thompson PJ, et al. Oral glucocorticoid-sparing effect of mepolizumab in eosinophilic asthma. *N Engl J Med*. 2014;371(13):1189-1197.
5. Han JK, Bachert C, Fokkens W, et al. Mepolizumab for chronic rhinosinusitis with nasal polyps (SYNAPSE): a randomized, double-blind, placebo-controlled, phase 3 trial. *Lancet Respir Med*. 2021;9(10):1141-1153.
6. Wechsler ME, Akuthota P, Jayne D. Mepolizumab or placebo for eosinophilic granulomatosis with polyangiitis. *N Engl J Med*. 2017;376(20):1921-1932.
7. 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.
8. Global Initiative for Asthma. Global strategy for asthma management and prevention. Updated 2025. Available at: <http://www.ginasthma.org>. Accessed on May 29, 2025.
9. Chung KF, Wenzel SE, Brozek JL, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J*. 2014;43:343-373.
10. Holguin F, Cardet JC, Chung KF, et al. Management of severe asthma: a European Respiratory Society/American Thoracic Society Guideline. *Eur Respir J*. 2020;55:1900588.
11. Rank MA, Chu DK, Bognanni A, et al. Joint Task Force on Practice Parameters GRADE guidelines for the medical management of chronic rhinosinusitis with nasal polyposis. *J Allergy Clin Immunol*. 2023;151(2):386-398.
12. Peters AT, Spector S, Hsu J, et al. Diagnosis and management of rhinosinusitis: a practice parameter update. *Ann Allergy Asthma Immunol*. 2014;347-385.
13. Dykewicz MS, Wallace DV, Baroody F, et al. Treatment of seasonal allergic rhinitis: an evidenced-based focused 2017 guideline update. *Ann Allergy Asthma Immunol*. 2017;119(6):489-511.
14. Joint Task Force on Practice Parameters: American Academy of Allergy, Asthma and Immunology and the American College of Allergy, Asthma and Immunology. Rhinitis 2020: a practice parameter update. *J Allergy Clin Immunol*. 2020;146:721-767.
15. Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, et al. Clinical practice guideline (update): adult sinusitis. *Otolaryngol Head Neck Surg*. 2015;152(2S):S1-S39.
16. Chung SA, Langford CA, Maz M, et al. 2021 American College of Rheumatology/Vasculitis Foundation guideline for the management of antineutrophil cytoplasmic antibody-associated vasculitis. *Arthritis Rheumatol*. 2021;73(8):1088-1105.
17. Hellmich B, Sanchez-Alamo B, Schirmer JH, et al. EULAR recommendations for the management of ANCA-associated vasculitis: 2022 update. *Ann Rheum Dis*. 2024;83(1):30-47.
18. Shomali W, Gotlib J. World Health Organization and international consensus classification of eosinophilic disorders: 2024 update on diagnosis, risk stratification, and management. *Am J Hematol*. 2024;99(5):946-968.
19. Oldhoff JM, Darsow U, Werfel T, et al. Anti-IL-5 recombinant humanized monoclonal antibody (mepolizumab) for the treatment of atopic dermatitis. *Allergy*. 2005;60(5):693-696.
20. Oldhoff JM, Darsow U, Werfel T, et al. No effect of anti-interleukin-5 therapy (mepolizumab) on the atopy patch test in atopic dermatitis patients. *Int Arch Allergy Immunol*. 2006;141(3):290-294.
21. Kang EG, Narayana PK, Pouliken IJ, et al. Efficacy and safety of mepolizumab administered subcutaneously for moderate to severe atopic dermatitis. *Allergy*. 2020;75(4):950-953.
22. Pavord ID, Chanez P, Criner GJ, et al. Mepolizumab for eosinophilic chronic obstructive pulmonary disease. *N Engl J Med*. 2017;377(17):1613-1629.
23. Sciurba FC, Criner GJ, Christenson SA, et al. Mepolizumab to prevent exacerbations of COPD with an eosinophilic phenotype. *N Engl J Med*. 2025;392:1710-1720.
24. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: 2025 report. Global Initiative for Chronic Obstructive Lung Disease. Available from: <http://goldcopd.org/>. Accessed on May 30, 2025.
25. Stein ML, Collins MH, Villanueva JM, et al. Anti-IL-5 (mepolizumab) therapy for eosinophilic esophagitis. *J Allergy Clin Immunol*. 2006;118(6):1312-1319.

26. Straumann A, Conus S, Grzonka P, et al. Anti-interleukin-5 antibody treatment (mepolizumab) in active eosinophilic esophagitis: a randomized, placebo-controlled, double-blind trial. *Gut*. 2010;59:21-30.
27. Assa'ad AH, Gupta SK, Collins MH, et al. An antibody against IL-5 reduces numbers of esophageal intraepithelial eosinophils in children with eosinophilic esophagitis. *Gastroenterology*. 2011;141(5):1593-1604.
28. Dallon ES, Peterson KA, Mitlyng BL, et al. Mepolizumab for treatment of adolescents and adults with eosinophilic oesophagitis: a multicenter, randomized, double-blind, placebo-controlled clinical trial. *Gut*. 2023;72(10):1828-1837.
29. Dallon ES, Muir AB, Katzka DA, et al. ACG Clinical Guideline: Diagnosis and Management of Eosinophilic Esophagitis. *Am J Gastroenterol*. 2025;120(1):31-59.
30. Wechsler ME, Nair P, Terrier B, et al. Benralizumab versus mepolizumab for eosinophilic granulomatosis with polyangiitis. *New Engl J Med*. 2024;390(10):911-921.

HISTORY

Type of Revision	Summary of Changes	Date Reviewed
Annual Revision	Conditions not recommended for approval: Criteria were updated to clarify that use of Nucala with another monoclonal antibody therapy is specific to Cinqair, Fasenra, Dupixent, Tezspire, Xolair, and Adbry.	03/22/2023
Selected Revision	Chronic Rhinosinusitis with Nasal Polyps: Approval condition updated from "Nasal Polyps" to "Chronic Rhinosinusitis with Nasal Polyps". Duration of the intranasal corticosteroid requirement was changed from 3 months to 4 weeks.	02/14/2024
Annual Revision	Asthma: Removed leukotriene receptor antagonists as an example of additional asthma controller or asthma maintenance medications.	04/19/2024
Selected Revision	Eosinophilic granulomatosis with polyangiitis: Criteria requiring the patient to have tried a minimum of 4 weeks of corticosteroid therapy were clarified to require the patient be currently receiving a systemic corticosteroid and have been on therapy for a minimum of 4 weeks.	07/17/2024
Selected Revision	Asthma: Eosinophil level requirements were clarified to require a level \geq 150 cells/microliter either within the previous 6 weeks OR prior to treatment with a monoclonal antibody that may alter eosinophil levels. Previously, criteria required a level \geq 150 cells/microliter either within the previous 6 weeks OR within 6 weeks prior to treatment with a monoclonal antibody that may lower eosinophil levels. Eosinophilic Granulomatosis with Polyangiitis: Initial approval duration was changed from 6 months to 9 months. Eosinophil level requirements were clarified to require a level \geq 150 cells/microliter either within the previous 4 weeks OR prior to treatment with a monoclonal antibody that may alter eosinophil levels. Previously, criteria required a level \geq 150 cells/microliter either within the previous 6 weeks OR within 6 weeks prior to treatment with a monoclonal antibody that may lower eosinophil levels. Hypereosinophilic Syndrome: Eosinophil level requirements were clarified that the level be taken prior to treatment with any monoclonal antibody therapy that may alter blood eosinophil levels. Previously, criteria required the level to be taken prior to any monoclonal antibody therapy that may lower blood eosinophil levels. Throughout the policy, Ebglyss (lebrikizumab-lbkz subcutaneous injection) and Nemluvio (nemolizumab-ilto subcutaneous injection) were added to notes as examples of monoclonal antibody therapies.	10/02/2024
Annual Revision	No criteria changes.	04/09/2025

HISTORY

Type of Revision	Summary of Changes	Date Reviewed
Early Annual Revision	<p>Chronic Obstructive Pulmonary Disease (COPD): This new condition and criteria for approval were added to the policy. New approval criteria for this indication were added that include an age requirement, an eosinophil requirement, a trial of inhaled therapies, a history of COPD exacerbations, and specialist involvement.</p> <p>Conditions Not Recommended for Approval, Chronic Obstructive Pulmonary Disease: Chronic Obstructive Pulmonary Disease was removed from the “Conditions Not Recommended for Approval”.</p>	06/04/2025
Selected Revision	<p>Chronic Rhinosinusitis with Nasal Polyps: Criteria were updated to require the patient has experienced symptoms for at least 8 weeks. Previously, criteria required the patient to have experienced symptoms for at least 6 months. A requirement that the patient has had the diagnosis of chronic rhinosinusitis with nasal polyps for at least 6 months was added. The requirement that the patient has received at least one course of treatment with a systemic corticosteroid was updated to require that the course of treatment has been within the previous year. Previously, criteria required that the course of treatment was for 5 days or more within the previous 2 years. A “Note” was added to clarify that one course of a systemic corticosteroid is ≥ 3 consecutive days of treatment or one long-acting injectable dose.</p>	11/05/2025