



Drug Coverage Policy

Effective Date.....8/1/2025

Coverage Policy Number IP0422

Policy Title.....Nucala

Immunologicals – Nucala

- Nucala® (mepolizumab subcutaneous injection – GlaxoSmithKline)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

OVERVIEW

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

- **Asthma**, as add-on maintenance treatment of patients ≥ 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 ≥ 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 ≥ 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 ≥ 12 years of age who have had HES for ≥ 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 ≥ 150 cells/microliter at screening or ≥ 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 ≥ 300 cells per microliter at screening and a level ≥ 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 ≥ 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).

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 stepwise 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 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.

Coverage Policy

Policy Statement

Prior Authorization is recommended for prescription benefit coverage of Nucala. All approvals are provided for the duration 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, approval requires Nucala to be prescribed by a physician who has consulted with or who specializes in the condition.

Nucala is considered medically necessary when ONE of are met (1, 2, 3, or 4):

FDA-Approved Indications

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 the following (i, ii, iii, iv, and v):

i. Patient is ≥ 6 years of age; AND

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

a) Patient has a blood eosinophil level ≥ 150 cells per microliter within the previous 6 weeks; OR

b) Patient has 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), Fasenra (benralizumab subcutaneous injection), Nemluvio (nemolizumab-ilto), Tezspire (tezepelumab-ekko subcutaneous injection), and 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 medium- or high- dose 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 a medium- or high- dose inhaled corticosteroid and additional asthma controller/maintenance medication(s) would fulfill the requirement for both criteria a and b.

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

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

(1) Patient has a forced expiratory volume in 1 second (FEV₁) $< 80\%$ predicted; AND

Note: The reduced FEV₁ should not be due to smoking-related chronic obstructive pulmonary disease.

(2) Patient has an FEV₁/forced vital capacity (FVC) < 0.80 ; OR

b) Patient meets ONE of the following (1, 2, 3, 4, or 5)

(1) Increase of $> 12\%$ and $> 200\text{ml}$ in FEV₁ following administration of a standard dose of a short-acting bronchodilator; OR

(2) Increase of $> 12\%$ and $> 200\text{ml}$ in FEV₁ between prescriber visits; OR

(3) Increase of $> 12\%$ and $> 200\text{ml}$ in FEV₁ from baseline to after at least 4 weeks of asthma treatment; OR

(4) Positive exercise challenge testing; OR

(5) Positive bronchial challenge testing; AND

Note: Patients 6 to 11 years of age would only be required to have an increase of $> 12\%$ in FEV₁ in each of the respective criteria above (i.e., they would not be required to have an increase $> 200\text{ mL}$)

Note: The above lung function criteria may be met at any time prior to or during asthma treatment.

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

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 asthma that worsens upon tapering of oral (systemic) corticosteroid therapy; AND

- vi. 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 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.

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-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 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.

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- 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 the following (i, ii, iii, iv, v, and vi):
 - i) Patient is ≥ 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 experienced two or more of the following symptoms for at least 6 months: nasal congestion, nasal obstruction, nasal discharge, and/or reduction/loss of smell; AND
 - iv) 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
- v) Patient meets ONE of the following (a, b, or c):
 - a) Patient has received at least one course of treatment with a systemic corticosteroid for 5 days or more within the previous 2 years; OR
 - b) Patient has a contraindication to systemic corticosteroid therapy; OR
 - c) Patient has had prior surgery for nasal polyps; AND
- vi) 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 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 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 ≥ 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) for a minimum of 4 weeks
 - 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), Fasenna (benralizumab subcutaneous injection), Nemluvio (nemolizumab-ilto), Tezspire (tezepelumab-ekko subcutaneous injection), and Xolair (omalizumab subcutaneous injection).
- ; AND

- 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 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 3A (Eosinophilic Granulomatosis with Polyangiitis, Initial Therapy).
- ii. Patient has responded to therapy as determined by the prescriber.
Note: Examples of 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.

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), Fasenna (benralizumab subcutaneous injection), Nemluvio (nemolizumab-ilto), Tezspire (tezepelumab-ekko subcutaneous injection), and 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 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 3A (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.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Nucala for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as newly published data are available):

- 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), Fasenra® (benralizumab subcutaneous injection), Nemluvio (nemolizumab-ilto), Teszipire® (tezepelumab-ekko subcutaneous injection), or Xolair® (omalizumab subcutaneous injection).
- 3. Eosinophilic Esophagitis, 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. Guidelines for the management of eosinophilic esophagitis from the American Gastroenterological Association (AGA) and the Joint Task Force on Allergy-Immunology Practice Parameters (2020) only recommend using anti-interleukin-5 therapies in the context of a clinical trial.²⁹ Further research is warranted to determine if Nucala has a place in therapy in the treatment of these conditions.

Coding Information

Note:

- 1) This list of codes may not be all-inclusive.
- 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J2182	Injection, mepolizumab, 1 mg

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.
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Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	<p>Updated coverage policy title from <i>Mepolizumab to Immunologicals – Nucala</i>.</p> <p><u>Asthma:</u> Updated diagnostic criteria requirements for confirmation of asthma.</p> <p>Updated initial approval authorization duration from 12 months to 6 months.</p> <p><u>EGPA:</u> Updated blood eosinophil count criteria for screening AEC greater than or equal to 150 cells/ mcL while stable on oral corticosteroid, only.</p>	9/1/2024

	<p>Updated initial approval authorization duration from 12 months to 6 months.</p> <p>Hypereosinophilic Syndrome: Updated initial approval authorization duration from 12 months to 8 months.</p>	
Selected Revision	<p>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.</p> <p>Eosinophilic granulomatosis with polyangiitis: Updated from " A.iii. Patient has tried therapy with a corticosteroid (e.g., prednisone) for a minimum of 4 weeks" to "A.iii.a) Patient is currently receiving has tried therapy with a systemic corticosteroid (e.g., prednisone) for a minimum of 4 weeks"</p> <p>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.</p> <p>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.</p> <p>Throughout the policy, Ebglyss (lebrikizumab-lbkz subcutaneous injection) and Nemludio (nemolizumab-ilto subcutaneous injection) were added to notes as examples of monoclonal antibody therapies.</p>	12/15/2024
Annual Revision	No criteria change.	7/15/2025

	Removed Ebglyss and Nemludio from examples of monoclonal antibody therapies for asthma.	
Selected Revision	<p>Chronic Obstructive Pulmonary Disease (COPD): This 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>	8/1/2025

The policy effective date is in force until updated or retired.

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