P&T Date: 08/07/2025

Nucala® (mepolizumab)

HCPCS: J2182

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved age
   b. For the diagnosis of severe uncontrolled eosinophilic asthma
      i. Patient is currently receiving, and will continue to receive standard of care regimen
      ii. Must be used as add on maintenance treatment with severe uncontrolled eosinophilic asthma
      iii. Severe eosinophilic asthma identified by:
         1. Blood eosinophils greater than or equal to 150 cells/microliter at initiation of treatment
      iv. Chronic administration of systemic corticosteroids or high dose inhaled corticosteroids (listed in table 1) in combination with
         1. Long acting inhaled β2 agonist for at least 3 months fails to maintain adequate control
            OR
         2. Leukotriene modifier for at least 3 months fails to maintain adequate control
            OR
         3. LAMA (long acting muscarinic antagonists) in adults and children ≥ 12 years old for at least 3 months fails to maintain adequate control

   OR
   c. Diagnosis of uncontrolled, moderate to severe chronic obstructive pulmonary disease (COPD)
      i. Patient is currently receiving, and will continue to receive standard of care regimen including LABA + LAMA + ICS, unless contraindicated
      ii. Evidence of type 2 inflammation (current eosinophils ≥ 150/µL OR eosinophils ≥ 300/µL within the past 12 months)

   OR
   d. A diagnosis of eosinophilic granulomatosis with polyangiitis (EGPA), and
      i. Documentation of a consult with an allergist/immunologist or pulmonologist prior to initiation of Nucala therapy
      ii. History or presence of asthma
      iii. At least 2 of the following criteria that are typical of EGPA
         1. Histopathological evidence of eosinophilic vasculitis, perivascular eosinophilic infiltration, or eosinophil-rich granulomatous inflammation
         2. Neuropathy
         3. Pulmonary infiltrates

4. Allergic rhinitis and nasal polyps
5. Cardiomyopathy
6. Glomerulonephritis
7. Alveolar hemorrhage
8. Palpable purpura
9. Antineutrophil cytoplasmic antibody (ANCA) positivity

OR

e. A diagnosis of hypereosinophilic syndrome (HES), and
    i. At least 2 HES flares within the past 12 months
        1. Defined as documented HES-related worsening of clinical symptoms or blood eosinophil counts requiring an escalation in therapy
    ii. Stable on HES therapy for at least 4 weeks
        1. Examples include oral corticosteroids, immunosuppressive or cytotoxic therapy
    iii. Eosinophil counts of 1,000 cells/microL or higher at initiation of therapy
    iv. Member does not have eosinophilia of unknown clinical significance, non-hematologic secondary HES (drug hypersensitivity, parasitic helminth infection, HIV infection, non-hematologic malignancy), or FIP1L1-PDGFRα kinase-positive HES

OR

f. A diagnosis of chronic rhinosinusitis with nasal polyps (CRSwNP)
    i. Patient is currently receiving, and will continue to receive standard of care regimen
    ii. Recurring severe CRSwNP despite previous treatment with intranasal corticosteroids
g. Not to be used in combination with other biologics or targeted disease-modifying antirheumatic drugs (DMARDs) for the same indication.
h. The member will self-administer Nucala unless clinically unable to do so
i. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in WyoBlue Advantage's utilization management medical drug list and/or the WyoBlue Advantage prior authorization and step therapy documents

B. Quantity Limitations, Authorization Period and Renewal Criteria
    a. Quantity Limits: Align with FDA recommended dosing
    b. Authorization Period: One year at a time
    c. Renewal Criteria: Clinical documentation must be provided to confirm that current criteria are met and that the medication is providing clinical benefit

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

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

- Add-on maintenance treatment of patients with severe asthma aged 6 years and older, and with an eosinophilic phenotype.
- The treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA).
- 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.
- Add-on maintenance treatment of adult patients with inadequately controlled chronic obstructive pulmonary disease (COPD) and an eosinophilic phenotype.
- Limitations of use: Not for relief of acute bronchospasm or status asthmaticus.

- Eosinophilic Granulomatosis with Polyangiitis (EGPA, formerly Churg-Strauss Syndrome)
  - Rare condition affecting 10-15 people per million
  - Mean age of diagnosis is 40 years old, and is rare in children, adolescents, and patients over 65
  - Antineutrophil cytoplasmic antibodies (ANCAs) are found in 40%-60% of patients, but it is unknown whether ANCAs have a pathogenic role or if this is simply a manifestation of EGPA
  - Multisystem disorder characterized by allergic rhinitis, asthma, and prominent peripheral blood eosinophilia
  - Primarily affects the lungs, followed by the skin, but also involves the cardiovascular, gastrointestinal, renal, and central nervous systems
  - Asthma is the cardinal feature of EGPA, which presents, along with allergic rhinitis and nasal polyps, long before vasculitis and the initial EGPA diagnosis
  - The next phase of the disease is typically eosinophilia, high levels of eosinophils in the blood, which are 5% or less in healthy patients and at least 10% up to as high as 60% in EGPA patients
  - Vasculitis is the third and final phase of symptoms and includes several organs: fever, fatigue, sudden weight loss, muscle and joint pain, rash, numbness/tingling/loss of strength of hands or feet, chest pain or palpitations, shortness of breath, chronic cough, venous thrombotic events, abdominal pain, blood in stool
  - Nucala is the first and only treatment available for adults with EGPA
- Hypereosinophilic syndrome (HES)
  - HES are a group of rare disorders marked by the sustained overproduction of eosinophils with an estimated prevalence between 0.36 to 6.3 per 100,000.
  - In HES, eosinophils damage the tissues that they infiltrate, with common targets that include skin, lung, and GI tract.
  - The goal of therapy is a reduction of the absolute eosinophil count, reduction of signs and symptoms, and prevention of disease progression.

- Choice of therapy depends on clinical features, specifically whether the patient has clinical features consistent with a myeloid disorder with or without a FIP1L1-PDGFRA positive mutation. Those with myeloid variants are treated initially with imatinib mesylate, while other types of HES are treated with an initial trial of glucocorticoids.

- Per the guideline for the investigation and management of eosinophilia in the British Journal of Haematology from January 2017, patients with idiopathic HES who do not respond adequately to corticosteroids, or who require prolonged corticosteroid therapy, or who are intolerant of corticosteroids, should be considered for a short trial (4 – 6 weeks) of imatinib, immunomodulatory agents (interferon alpha, ciclosporin or azathioprine), myelosuppressive therapy (hydroxycarbamide) or monoclonal antibody therapy with mepolizumab (anti-interleukin 5), the latter preferably as part of a clinical trial (Grade 2B).

- Prednisone is the primary initial therapy for symptomatic FIP1L1-PDGFRA-negative HES without indications for emergency treatment. Appropriate starting doses range from 20 mg to 60 mg daily, depending on the severity of the disease manifestations and the degree of eosinophilia at presentation. The dose should be adjusted once the patient responds. Once blood eosinophilia is suppressed and symptoms are controlled, daily glucocorticoid doses are gradually reduced to the lowest dose that maintains control of the eosinophil count and clinical manifestations. Alternate-day dosing should be the ultimate goal if tolerated.

- Hypereosinophilia of unknown significance (HEus) patients are asymptomatic but have marked eosinophilia (>1,500 cells/microL) and no evidence of clinical manifestations or organ involvement. HEus is not considered a form of HES as eosinophil-mediated complications are absent.

- Those individuals included in Nucala's pivotal trial for HES had eosinophil counts greater than 1,000 cells/microL during screening, a history of 2 or more flares within the past 12 months and had been stable on HES therapy for at least 4 weeks prior to randomization.

– Severe asthma with an eosinophilic phenotype

  - Severe asthma requires treatment with high dose inhaled corticosteroids (ICS) plus a second controller (and/or systemic corticosteroids) to prevent it from becoming uncontrolled or which remains uncontrolled despite therapy. Add-on treatment for severe asthma include LAMA, leukotriene receptor antagonist (LTRA), low dose azithromycin (adults) and biologic agents for severe allergic or severe type 2 asthma. Type 2 inflammation is found in a majority of people with severe asthma and characterized by production of cytokines such as interleukin (IL). Anti-IL5 monoclonal antibodies (Cinqair®, Nucala, and Fasenra™) specifically target the formation of eosinophils and deplete blood eosinophil levels.

  - The Global Institute for Asthma (GINA) 2023 Difficult-to-Treat & Severe Asthma Diagnosis and Management guidelines recommend those with sever asthma and Type 2 airway inflammation (blood eosinophils ≥ 150/µL and/or fractional exhaled nitric oxide (FeNO) ≥20 ppb and/or sputum eosinophils ≥2%, and/or asthma is clinically allergen driven) first should consider adherence tests and consider increasing the ICS dose for 3-6 months. Add-on Type 2-targeted biologic therapy should be considered for patients with exacerbations or poor symptom control on high dose ICS-LABA. Local payer eligibility criteria, comorbidities should also be considered. Anti-IL5/anti-IL5R, including Nucala is appropriate in patients with exacerbations in the last year and blood eosinophils ≥ 150/µL.

  - A peripheral blood eosinophil count is an indirect way to estimate airway inflammation. A blood eosinophil count ≥ 300 cells/microL may help predict asthmatics who are at increased risk for exacerbations in the next year. Furthermore, a count-response relation exists between blood eosinophil counts and asthma-related outcomes. The European Respiratory Society/American Thoracic Society guidelines from 2020 suggest that treatment of severe asthma be guided by clinical criteria and biomarkers such as blood eosinophil levels or

fractional exhaled nitric oxide (FeNO), rather than by clinical criteria alone. In addition, it also suggests that a blood eosinophil count cut-off point of ≥ 150 cells/microliter can be used to guide anti-IL5 initiation in adult patients with severe asthma and a history of prior asthma exacerbations.

- Response to biologic therapy is reviewed after 3-4 months of treatment. If the patient had a good response, the need for each medication should re-evaluated, but do not completely stop inhaled therapy. Consider gradually decreasing or stopping oral steroids first.

- Chronic rhinosinusitis with nasal polyps

  - Chronic rhinosinusitis with nasal polyps (CRSwNP, also referred to as nasal polyposis or nasal polyps) is a chronic inflammatory disease of the nasal passage lining or sinuses that leads to bilateral, benign soft tissue growth referred to as nasal polyps. It affects 5% - 12% of the general population worldwide, often occurring with other immunologic conditions such as allergies and/or asthma. The polyps are characterized by elevated eosinophil levels and are most commonly seen in the third and fourth decade of life.

  - The cornerstone of treatment for nasal polyps is intranasal corticosteroids as well as nasal saline sprays or irrigation. Systemic corticosteroids may also be used short term (10-15 days) to reduce severe polyp inflammation and symptoms like impaired sense of smell or severe nasal blockage.

  - For patients with refractory disease that has not responded to intranasal and oral corticosteroids, biologic therapy and/or functional endoscopic sinus surgery (FESS) may be considered. Surgery must be followed with maintenance therapy with intranasal corticosteroids and other appropriate therapies to prevent recurrence of polyps. No comparative studies or guidelines are available that recommend one treatment option over another for refractory cases.

  - Maintenance therapies are initiated once symptoms have been controlled to minimize inflammation and prevent the regrowth of nasal polyps after surgery. The mainstay of maintenance treatment is intranasal glucocorticoids. Leukotriene inhibitors may also be of benefit as adjunctive therapy, particularly if allergic rhinitis or aspirin-exacerbated respiratory disease are suspected contributing factors.

- COPD with an eosinophilic phenotype

  - The 2025 Global Initiative for Chronic Obstructive Lung Disease (GOLD) Report ("GOLD guideline") defines COPD as a heterogeneous lung condition characterized by chronic respiratory symptoms (dyspnea, cough, sputum production, and/or exacerbations) due to abnormalities of the airways (bronchitis, bronchiolitis) and/or alveoli (emphysema) that cause persistent, often progressive airflow obstruction. As the definition states, COPD includes chronic bronchitis and/or emphysema, which both make emptying air from the lungs progressively more difficult. Most people with COPD have a combination of both conditions. Dyspnea is the most common symptom of COPD; however, chronic cough and sputum production are also cardinal symptoms. COPD is a common, chronic lung disease. It is estimated that 16 million people in the United States have COPD, which represents a prevalence of about 6% among adults. COPD is almost exclusively diagnosed in adulthood, typically in adults over the age of 40 years. However, factors/exposures from childhood (e.g. premature birth, respiratory infections, secondhand smoke) are thought to play a role in the future development of COPD in some patients. The prevalence of COPD increases with age, with an estimated prevalence of over 12% in the 65 years of age and older population. COPD is slightly more common in women than men.

  - The GOLD guideline's (2025) initial treatment algorithm for COPD is individualized based on an assessment of the patient's symptoms and exacerbation history. These assessments determine the suggested treatment

option for patients. Initial pharmacologic treatment includes either a bronchodilator, LABA + LAMA, or LABA + LAMA + ICS depending on a patient's symptoms and exacerbation history. LABA + LAMA + ICS should be considered if blood eosinophils are ≥ 300/µL. Among those with eosinophils ≥ 300/µL and symptoms of chronic bronchitis, consider adding dupilumab (Dupixent®). If a patient's response to initial treatment is appropriate, they should be maintained on that treatment. If a patient does not respond to initial treatment, then adherence, inhaler technique, and possible interfering comorbidities should be checked. Follow-up pharmacologic treatment follows a stepwise approach and is determined based on whether dyspnea or exacerbations are the predominant treatable trait to target. If dyspnea is the predominant trait a patient should start with either a LAMA or LABA and should progress to LABA + LAMA. If exacerbations are the predominant trait, then patients should start with a LABA or LAMA, progress to LABA + LAMA (+ICS if blood eosinophil count ≥ 300 cells/µL) and eventually add on roflumilast (if FEV1 <50% and chronic bronchitis) or add azithromycin (preferred in former smokers). Of note, Nucala has not been included in the GOLD guidelines at this time.

- During Phase III trials, Nucala was evaluated in patients with COPD and an eosinophilic phenotype (blood eosinophil count [BEC] ≥150 cells/µL); Dupixent was evaluated in patients with a BEC ≥300 cells/µL. GSK notes that ~70% of U.S. patients with COPD who continue to experience exacerbations on inhaled triple therapy have a BEC ≥150 cells/µL, representing over one million people.

- There have been no studies supporting co-administration of Nucala with other biologics for approved indications, therefore the safety and efficacy of Nucala in unknown when used in combination with other biologics.

- Clinical reasons a patient may be unable to self-administer Nucala include:

  - Patient or caregivers are unable to perform subcutaneous injections with proper technique

  - Member requires monthly medical support from the physician

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Table 1: Comparative cumulative daily dosing of inhaled corticosteroids (mcg/day)

	Ages 12 and up	Ages 6-11

Inhaled Corticosteroid	Low Dose	Medium Dose	High Dose	Low Dose	Medium Dose	High Dose
Beclomethasone dipropionate HFA	100 – 200	>200 – 400	>400	50 – 100	>100 – 200	>200
Budesonide DPI	200 – 400	>400 – 800	>800	100 – 200	>200 – 400	>400
Budesonide nebules	NA	NA	NA	250 – 500	>500 – 1,000	>1,000
Ciclesonide HFA	80 – 160	>160 – 320	>320	80	>80 – 160	>160
Fluticasone furoate DPI	100	NA	200	NA	NA	NA
Fluticasone propionate DPI	100 – 250	>250 – 500	>500	100 – 200	>200 – 400	>400
Fluticasone propionate HFA	100 – 250	>250 – 500	>500	100 – 200	>200 – 500	>500
Mometasone furoate	110 – 220	>220 – 440	>440	110	≥220 - <440	≥440
Triamcinolone acetonide	400 – 1,000	>1,000 – 2,000	>2,000	400 – 800	>800 – 1,200	>1,200

Policy History		
#	Date	Change Description
1.0	Initial Effective Date: 01/01/2026	New policy

** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*