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Mepolizumab

Table of Contents

Related Policies (if applicable)
None

Disclaimer

Medical policies are a set of written guidelines that support current standards of practice. They are based on current peer-reviewed scientific literature. A requested therapy must be proven effective for the relevant diagnosis or procedure. For drug therapy, the proposed dose, frequency and duration of therapy must be consistent with recommendations in at least one authoritative source. This medical policy is supported by FDA-approved labeling and/or nationally recognized authoritative references to major drug compendia, peer reviewed scientific literature and acceptable standards of medical practice. These references include, but are not limited to: MCG care guidelines, DrugDex (IIa level of evidence or higher), NCCN Guidelines (IIb level of evidence or higher), NCCN Compendia (IIb level of evidence or higher), professional society guidelines, and CMS coverage policy.

Carefully check state regulations and/or the member contract.

Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Legislative Mandates

EXCEPTION: For HCSC members residing in the state of Ohio, § 3923.60 requires any group or individual policy (Small, Mid-Market, Large Groups, Municipalities/Counties/Schools, State Employees, Fully-Insured, PPO, HMO, POS, EPO) that covers prescription drugs to provide for the coverage of any drug approved by the U. S. Food and Drug Administration (FDA) when it is prescribed for a use recognized as safe and effective for the treatment of a given indication in one or more of the standard medical reference compendia adopted by the United States Department of Health and Human Services or in medical literature even if the FDA has not approved the drug for that indication. Medical literature support is only satisfied when safety and efficacy has been confirmed in two articles from major peer-reviewed professional medical journals that present data supporting the proposed off-label use or uses as generally safe and effective. Examples of accepted journals include, but are not limited to, Journal of

American Medical Association (JAMA), New England Journal of Medicine (NEJM), and Lancet. Accepted study designs may include, but are not limited to, randomized, double blind, placebo controlled clinical trials. Evidence limited to case studies or case series is not sufficient to meet the standard of this criterion. Coverage is never required where the FDA has recognized a use to be contraindicated and coverage is not required for non-formulary drugs.

Coverage

Eosinophilic Asthma

Mepolizumab (Nucala®) **may be considered medically necessary** for the treatment of severe eosinophilic asthma when the following criteria are met:

- Individual is 6 years of age or older; AND
- There is documented and current use of an inhaled corticosteroid (ICS) in combination with a long acting beta2-agonist (LABA), leukotriene receptor antagonist [LTRA], theophylline or long-acting muscarinic antagonist (LAMA) for at least 3 months; AND
- The individual has uncontrolled asthma while on control therapy as evidenced by two or more exacerbations requiring systemic glucocorticoids, frequent ER visits, or hospitalizations (see **NOTE 1**); AND
- Eosinophil count of the following (in the absence of other potential causes of eosinophilia, including hypereosinophilic syndromes, neoplastic disease, and known or suspected parasitic infection):
  - 150 cells/µL or more in peripheral blood at screening; or
  - 300 cells/µL or more during the previous year; AND
- Will not be used in combination with another antiasthmatic monoclonal antibody agent (e.g., omalizumab [Xolair], benralizumab [Fasenra], reslizumab [Cinqair]).

NOTE 1: Individuals who do not meet the criteria for uncontrolled asthma, but whose asthma worsens on tapering off corticosteroids, will also meet this definition of moderate to severe asthma. For definition of uncontrolled asthma see Description section.

NOTE 2: 1 microliter (ul) is equal to 1 cubic millimeter (mm^3).

Hypereosinophilic Syndrome

Mepolizumab (Nucala®) **may be considered medically necessary** for the treatment of hypereosinophilic syndrome (HES) when the following criteria are met:

- Individual is 12 years of age or older; AND
- Individual is ≥ 6 months without an identifiable non-hematologic HES or FIP1L1-PDGFRα kinase-positive HES; AND
- History of 2 or more HES flares within the past 12 months; AND
- Blood eosinophil count of 1,000 cells/mcL or higher at screening.

NOTE 3: A HES flare is defined as HES-related worsening of clinical symptoms or increasing blood eosinophil counts (on at least 2 occasions) requiring an escalation in therapy (HES

therapy could include chronic or episodic oral corticosteroids (OCS), immunosuppressive, or cytotoxic therapy).

NOTE 4: Non-hematologic HES may include drug hypersensitivity, parasitic helminth infection, human immunodeficiency virus (HIV) infection, non-hematologic malignancy.

Eosinophilic Granulomatosis with Polyangiitis

Mepolizumab (Nucala®) **may be considered medically necessary** for the treatment of relapsing or refractory eosinophilic granulomatosis with polyangiitis (EGPA) (Churg-Strauss syndrome) when the following criteria are met:

- Individual is 18 years of age or older; AND
- Diagnosis of relapsing or refractory EGPA for 6 months or greater, defined as:
  - A history or presence of asthma; and
  - Blood eosinophil level of >10% of leucocytes or an absolute eosinophil count of greater than 1000 cells per cubic millimeter (mm^3) (in the absence of other potential causes of eosinophilia, including hypereosinophilic syndromes, and known suspected parasitic infection); and
  - Presence of two or more of the following features of EGPA:
    1) A biopsy showing histopathological evidence of:
       a) Eosinophilic vasculitis; or
       b) Perivascular eosinophilic infiltration; or
       c) Eosinophil-rich granulomatous inflammation;
    2) Neuropathy, mono or poly (motor deficit or nerve conduction abnormality);
    3) Pulmonary infiltrates, non-fixed;
    4) Sino-nasal abnormality;
    5) Cardiomyopathy (established by echocardiography or magnetic resonance imaging);
    6) Glomerulonephritis (hematuria, red cell casts, proteinuria);
    7) Alveolar hemorrhage (by bronchoalveolar lavage);
    8) Palpable purpura; or
    9) Antineutrophil cytoplasmic antibody (ANCA) positive (Myeloperoxidase or proteinease 3); and
  - History of relapsing or refractory disease defined as one of the following:
    1) Relapsing disease defined as history (within the past 2 years) of at least one EGPA relapse (requiring additional or dose escalation of corticosteroids or immunosuppressant, or hospitalization); or
    2) Refractory disease defined as failure to attain remission within the prior 6 months following induction treatment with a standard therapy regimen (e.g., cyclophosphamide, methotrexate, azathioprine, mycophenolate mofetil, high-dose corticosteroids), administered for at least 3 months; or within 6 months prior to initiation, recurrence of symptoms of EGPA while tapering oral corticosteroids (OCS), occurring at any dose level $\geq$ 7.5 mg/day prednisolone or equivalent.

Chronic Rhinosinusitis with Nasal Polyps

Mepolizumab (Nucala®) **may be considered medically necessary** for the treatment of chronic rhinosinusitis with nasal polyps (CRSwNP) when the following criteria are met:

- Individual is 18 years of age or older; AND
- Confirmation of diagnosis by one of the following:
  - Anterior rhinoscopy or endoscopy; or
  - Computed tomography (CT) of the sinuses; AND
- One of the following:
  - Inadequate response, intolerance, or contraindication to intranasal corticosteroids; or
  - Inadequate response to prior sinonasal surgery; AND
- Will be used in combination with standard nasal polyp maintenance therapy (e.g., nasal saline irrigation, intranasal corticosteroids); AND
- Will not be used in combination with other monoclonal antibodies for the treatment of nasal polyps (e.g., omalizumab [Xolair], dupilumab [Dupixent]).

Mepolizumab (Nucala®) **is considered experimental, investigational and/or unproven** when not meeting criteria as outlined above and for all other indications, including but not limited to:

- Eosinophilic chronic obstructive pulmonary disease;
- Eosinophilic esophagitis; and
- Urticaria.

Self-Administration

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage of a formulation that cannot be self-administered **may be considered medically necessary** when:

- Patient or caregiver is unable to recognize symptoms of anaphylaxis; OR
- Patient or caregiver is unable to treat anaphylaxis appropriately; OR
- Patient or caregiver is unable to perform subcutaneous injections with a prefilled syringe or autoinjector with proper technique according to the prescribed dosing regimen and Instructions for Use; OR
- The patient has a physical or cognitive limitation that makes the utilization of a self-administered formulation unsafe or otherwise not feasible, as demonstrated by BOTH of the following:
  - Inability to self-administer the medication; and
  - Lack of caregiver or support system for assistance with administration of self-administered products

Coverage of a formulation that cannot be self-administered **is considered not medically necessary** if the above criteria are not met.

Policy Guidelines

None.

Description

Asthma affects about 300 million people worldwide and more than 27 million in the United States. (1) In most cases, it can be effectively controlled with standard treatment that includes short-acting β2-agonists, long-acting β2-agonists (LABA), inhaled corticosteroids (ICSs), oral corticosteroids, and omalizumab if allergies present. However, 5% to 10% of patients suffer from severe or refractory asthma who cannot achieve control with standard treatment.

Much remains unclear about the best approaches to managing severe asthma and specifically eosinophilic asthma. Patients with eosinophilic asthma are generally responsive to corticosteroid therapy and are at an increased risk of exacerbation after corticosteroid withdrawal. In contrast, non–eosinophilic asthma is associated with a significantly poorer response to treatment with ICSs. New treatments, particularly monoclonal antibodies currently being developed, target specific pathophysiologic mechanisms, and therefore must be tailored to each patient to match the disease heterogeneity.

Definition of Uncontrolled Asthma

At least one of the following:

- Asthma Control Questionnaire (ACQ) score consistently >1.5, Asthma Control Test (ACT) score <20 (or ‘‘not well controlled’’ by National Asthma Education and Prevention Program (NAEPP) /Global Initiative for Asthma (GINA) guidelines);
- Frequent severe exacerbations: ≥2 bursts of systemic corticosteroids (CS) (>3 days each) in the previous year;
- Serious exacerbations: at least 1 hospitalization, ICU stay, or mechanical ventilation in the previous year;
- Airflow limitation: after appropriate bronchodilator withhold, forced expiratory volume in 1 second (FEV_1) <80% predicted (in the face of reduced FEV_1/forced vital capacity (FVC) defined as less than the lower limit of normal). (2)

Eosinophilic granulomatosis with polyangiitis (EGPA) (Churg-Strauss syndrome) is characterized by asthma, sinusitis, pulmonary infiltrates, neuropathy, and eosinophilic vasculitis of one or more end-organs. (3) Eosinophils are thought to induce pathogenic effects in patients with eosinophilic granulomatosis with polyangiitis by means of tissue and vascular infiltration and inflammation through a variety of mediators.

Hypereosinophilic Syndrome (HES) is a group of rare blood disorders. It occurs when an individual's blood has very high numbers of eosinophils. (4) An eosinophil is a type of white blood cell that plays an important role in the immune system. These eosinophils make their way into various tissues, causing inflammation and eventually organ dysfunction. The most commonly involved organs in HES include the skin, lungs, heart and nervous system. The goal of HES treatment is to reduce eosinophil levels in the blood and tissues, thereby preventing tissue damage–especially in the heart. Standard HES treatment includes glucocorticosteroid

medications such as prednisone, and chemotherapeutic agents such as hydroxyurea, chlorambucil and vincristine. Interferon-alpha may also be used as a treatment. This medication must be administered by frequent injections. The prognosis of HES depends upon the extent of any organ damage. Although survival rates have improved significantly, HES may be fatal in very severe cases. In 1975, only 12% of HES patients survived three years. Today, more than 80% of HES patients survive five years or more.

Chronic rhinosinusitis (CRS) can be broadly defined as an inflammatory disorder of the paranasal sinuses and linings of the nasal passages that lasts 12 weeks or longer. Signs and symptoms include anterior and/or posterior nasal mucopurulent drainage; nasal obstruction, blockage, or congestion; facial pain, pressure and/or fullness; and reduction or loss of sense of smell. About 20%-33% of cases include nasal polyposis and is characterized gradual worsening of nasal congestion/obstruction, sinus fullness and pressure, fatigue, posterior nasal drainage and partial or complete loss of sense of smell. Physical examination shows the presence of bilateral nasal polyps in the middle meatus. Nasal polyps are translucent, yellowish-gray to white, glistening masses composed of gelatinous inflammatory material, which may form in the nasal cavity or paranasal sinuses. Asthma is more strongly associated with chronic rhinosinusitis with nasal polyposis than CRS without nasal polyposis. (5)

Mepolizumab (Nucala)
Mepolizumab (GlaxoSmithKline) is a humanized immunoglobulin G1 (IgG1) monoclonal antibody specific to interleukin-5 (IL-5), which binds to IL-5, stopping IL-5 from binding to its receptor on the surface of eosinophils. Inhibiting IL-5 binding in this way reduces blood, tissue, and sputum eosinophil levels.

Regulatory Status
- On November 4, 2015, the U. S. Food and Drug Administration (FDA) approved mepolizumab (Nucala®) as an add-on maintenance therapy for patients aged 12 years or older who have severe eosinophilic asthma with a history of exacerbations.
- On December 12, 2017, the FDA revised their label to include the indication of EGPA.
- On September 12, 2019, the FDA approved mepolizuman (Nucala) for 6 to 11 year old children with severe eosinophilic asthma.
- On September 25, 2020, the FDA approved mepolizumab as the first the first and only biologic treatment for hypereosinophilic syndrome (HES).
- In July 29, 2021, the FDA approved mepolizumab (Nucala) for use in adults with chronic rhinosinusitis with nasal polyps. (6)

Rationale

This policy was created in 2016 and based on the U.S. Food and Drug Administration (FDA)-approved label and published literature. The most recent literature update was performed through January 24, 2024.

Mepolizumab (Nucala®) for Severe Eosinophilic Asthma (7)

Adult and Adolescent Population Aged 12 Years and Older

The evidence consists of one phase 2b dose-finding trial (DREAM) and two phase 3 trials (MENSA, SIRIUS). All 3 were randomized, double-blind, placebo-controlled, parallel-design trials.

DREAM

The DREAM trial (N=621) had 2 main objectives: 1) to assess the most efficacious dose of mepolizumab between 75, 250, and 750 mg monthly, and 2) to identify a less invasive biomarker that could be more applicable in clinical practice than induced sputum to assess eosinophilic airway inflammation.

In the DREAM trial, all 3 doses of mepolizumab had an equivalent clinical effect and therefore allowed study investigators to pool data across the 3 dose arms to investigate baseline factors associated with a treatment response with adequate power. History of prior asthma exacerbation and the baseline blood eosinophil above $0.15x10^9$/L were the strongest predictors of response. Therefore, in subsequent confirmatory MENSA and SIRIIUS trials, eosinophil blood counts of 150 cells/µL or higher in peripheral blood instead of sputum eosinophil counts was used as inclusion criteria to select patients with eosinophilic airway inflammation. Because the lowest dose of 75 mg intravenous (IV) studied in the DREAM trial was as effective as the higher dose, evaluation of a subcutaneous (SC) dose in the subsequent MENSA trial was tested as a possible alternative. Regarding efficacy, compared with placebo, all 3 doses of mepolizumab reduced clinically significant exacerbations by similar proportions (mepolizumab 75 mg by 48%, mepolizumab 250 mg by 39%, mepolizumab 750 mg by 52%).

MENSA

The objective of the MENSA trial (N=580) was to evaluate 2 doses of mepolizumab 75 mg IV and 100 mg SC and to compare them with placebo to assess whether mepolizumab decreases the annualized rate of asthma exacerbations. Regarding efficacy, compared with placebo, both 75 mg IV or 100 mg SC mepolizumab reduced clinically significant exacerbations (75 mg IV by 47% and 100 mg SC by 53% vs placebo). A prespecified analysis of clinical end points in a subgroup of patients with a blood eosinophil count of 500 cells/µL or more showed an enhanced response to mepolizumab. Compared with placebo, both 75 mg IV or 100 mg SC mepolizumab reduced clinically significant exacerbations (75 mg IV by 74% and 100 mg SC by 80% vs placebo) in 177 patients with blood eosinophil count of 500 cells/µL or more. The annualized rates of asthma exacerbation in mepolizumab 75 mg IV, mepolizumab 100 mg SC, and placebo were 0.58, 0.46, and 2.26, respectively.

SIRIUS

The objective of the SIRIUS trial (N=135) was to assess whether adjunctive treatment with 100 mg SC mepolizumab could reduce use of maintenance oral glucocorticoids while maintaining asthma control. In the MENSA trial, 25% of patients randomized were using daily oral glucocorticoids while in the SIRIUS trial 100% patients were. The trial design consisted of 4 distinct phases; optimization, induction, reduction, and maintenance:

- In the run-in optimization phase, the oral glucocorticoid dose was reduced weekly over 3 to 8 weeks until there was an exacerbation in asthma symptoms or a worsening in asthma control. Patients then underwent randomization and entered the next phase.
- In the induction phase (from week 0 through week 4), patients received the assigned study drug plus the optimized dose of oral glucocorticoids.
- In the reduction phase (from week 4 through 20), the oral glucocorticoid dose was reduced according to a prespecified schedule by 1.25 to 10 mg/d every 4 weeks on the basis of asthma control and symptoms of adrenal insufficiency.
- In the maintenance phase (from week 20 through week 24), no further adjustment was made in the oral glucocorticoid dose.

The authors of the SIRIUS trial reported an odds ratio (OR) of 2.39 (95% confidence interval [CI], 1.25 to 4.56) in favor of mepolizumab versus placebo in reducing daily oral glucocorticoid dose (>0% to 100%) versus no decrease in oral glucocorticoid dose, a lack of asthma control, or withdrawal from treatment. Given frequent reductions in the placebo arm, the OR is substantively larger than the estimated relative risk (RR). For example, the proportion of patients who experienced daily oral glucocorticoid dose reduction between more than 0% and 100% was 64% (44/69) and 44% (29/66) in the mepolizumab 100 mg SC and placebo groups, respectively, with an RR of 1.45 (95% CI, 1.05 to 2.01) and absolute risk reduction (ARR) of 19.8% (95% CI, -35.2% to -3%). Although optimizing the oral glucocorticoid dose at baseline and reducing the glucocorticoid dose in a standardized fashion, 44% of those receiving placebo were able to reduce their asthma doses between more than 0% and 100%, with 34% of patients reducing their doses by more than 50%. It is impossible to determine whether the effect seen in the control arm was a placebo effect, natural history, or other nonspecific effect. The authors noted that the placebo effect seen in the SIRIUS trial was lower than the placebo effect seen in other glucocorticoid reduction studies using mepolizumab, methotrexate, and cyclosporine. Reductions of 50% compared with reductions less than 49% were more than twice as frequent with mepolizumab as with placebo (40% vs 19%). ARR was 20% but accompanied by a CI (a high of 35% to a low as 3%) suggesting uncertainty in the estimate. The annualized rates of exacerbations were 1.44 per year in the mepolizumab group and 2.12 per year in the placebo group. (7)

Pediatric Population Aged 6 to 11 Years

The safety data for mepolizumab is based upon 1 open-label clinical trial that enrolled 36 subjects with severe asthma aged 6 to 11 years. Subjects received 40 mg (for those weighing <40 kg) or 100mg (for those weighing $\geq$ 40 kg) of mepolizumab administered SC once every 4 weeks. Subjects received mepolizumab for 12 weeks (initial short phase). After a treatment interruption of 8 weeks, 30 subjects received mepolizumab for a further 52 weeks (long phase). The adverse reaction profile for subjects aged 6 to 11 years was similar to that observed in subjects aged 12 years and older. The efficacy of mepolizumab in children aged 6 to 11 years is extrapolated from efficacy in adults and adolescents with support from pharmacokinetic analyses showing similar drug exposure levels for 40 mg administered SC every 4 weeks in children aged 6 to 11 years compared with adults and adolescents. (7)

Mepolizumab (Nucala®) for Hypereosinophilic Syndrome (HES)

Use of mepolizumab for HES is supported by evidence from an adequate and well-controlled study (NCT02836496) in adults and adolescents and an open-label extension study (NCT03306043). A total of 108 adult and adolescent patients aged 12 years and older with HES for at least 6 months were evaluated in a randomized, double-blind, placebo-controlled, multicenter, 32-week trial (NCT02836496). Patients with non-hematologic secondary HES (e.g., drug hypersensitivity, parasitic helminth infection, human immunodeficiency virus (HIV) infection, non-hematologic malignancy) or FIP1L1-PDGFRα kinase-positive HES were excluded from the trial. Patients received 300 mg of mepolizumab or placebo SC once every 4 weeks while continuing their stable HES therapy. Patients entering the trial had experienced at least 2 HES flares within the past 12 months and a blood eosinophil count of 1,000 cells/mcL or higher during screening. Historical HES flares for the trial entry criteria were defined as HES-related worsening of clinical symptoms or blood eosinophil counts requiring an escalation in therapy. Patients must have been on stable HES therapy for the 4 weeks prior to randomization. HES therapy could include chronic or episodic oral corticosteroids (OCS), immunosuppressive, or cytotoxic therapy. The efficacy of mepolizumab in HES was established based upon the proportion of patients who experienced a HES flare during the 32-week treatment period. A HES flare was defined as worsening of clinical signs and symptoms of HES or increasing eosinophils (on at least 2 occasions), resulting in the need to increase OCS or increase/add cytotoxic or immunosuppressive HES therapy. The trial compared the proportion of patients who experienced a HES flare or withdrew from the trial in the mepolizumab and placebo treatment groups. Over the 32-week treatment period, the incidence of HES flare over the treatment period was 56% for the placebo group and 28% for the group treated with mepolizumab (50% reduction). (7)

Mepolizumab (Nucala®) for Relapsing or Refractory Eosinophilic Granulomatosis with Polyangiitis (EGPA)

In 2017, Wechsler et al. published a 52-week multicenter, double-blind, parallel-group, phase 3 trial. (3) The reviewers randomly assigned participants of at least 18 years of age with a diagnosis of relapsing or refractory EGPA who had received treatment for at least 4 weeks and were taking a stable prednisolone or prednisone dose, to receive 300 mg of mepolizumab (n=68) or placebo (n=68), administered SC every 4 weeks, in addition to standard care (glucocorticoid treatment, with or without immunosuppressive), for 52 weeks, followed by 8 weeks of follow-up. The two primary end points were accrued weeks or remission over a 52-week period and the proportion of participants in remission at both week 36 and week 48. Secondary end points included the time to first relapse and the average daily glucocorticoid dose (during weeks 48 through 52). Participants receiving mepolizumab treatment achieved significantly more accrued weeks of remission than placebo (28% vs 3% of the participants had $\geq$ 24 weeks of accrued remission; OR, 5.91; 95% CI, 2.68 to 13.03; P<0.001) and a higher percentage of participants in remission at both week 36 and week 48 (32% vs 3%; OR, 16.74; 95% CI, 3.61 to 77.56; P<0.001). The participants in the placebo group did not achieve remission in 81% versus 47% of those in the mepolizumab group. The mepolizumab group had an annualized relapse rate of 1.14, as compared with 2.27 in the placebo group (rate ratio, 0.50; 95% CI, 0.36 to 0.70; P<0.001). Forty-four percent of the participants in the mepolizumab group

had an average daily dose of prednisolone or prednisone of 4.0 mg of less per day compared with 7% of those in the placebo group during weeks 48 through 52 (OR, 0.20; 95% CI, 0.09 to 0.41; P<0.001. The safety profile of mepolizumab was similar to that observed in studies of mepolizumab for eosinophilic asthma. There was no significant difference between the mepolizumab group and the placebo group in the percentage of participants who had an adverse event (97% and 94% respectively, there was an imbalance with regard to serious adverse events during the trial period (18% vs 2.6%). The most commonly reported adverse events were headache (in 32% of the participants in the mepolizumab group and 18% of those in the placebo group) nasopharyngitis (in 18% and 24%, respectively), arthralgia (in 22% and 18%, sinusitis (in 21% and 16%, and upper respiratory tract infection (in 21% and 16%). The reviewers concluded that participants with eosinophilic granulomatosis with polyangiitis, mepolizumab resulted in significantly more weeks in remission and a higher proportion of participants in remission than did placebo.

Mepolizumab (Nucala®) for Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)
A total of 407 adult patients with CRSwNP were evaluated in a randomized, double-blind, placebo-controlled, multicenter, 52-week trial (NCT03085797). Patients received Nucala 100 mg or placebo administered subcutaneously once every 4 weeks while continuing nasal corticosteroid therapy. Patients must have received background nasal corticosteroid for ≥8 weeks pre-screening. Patients had recurrent and symptomatic CRSwNP and had at least 1 surgery for the removal of nasal polyps within the previous 10 years. Patients were required to have nasal obstruction symptoms with a visual analog scale (VAS) score of >5 out of a maximum score of 10. Patients were also required to have an endoscopic bilateral nasal polyp score (NPS) of ≥5 out of 8 with NPS ≥2 in each nasal cavity. Patients reported nasal obstruction VAS scores daily by placing a single mark on a continuous line labeled from 0 (none) to 100 (as bad as you can imagine). The distance along the line was converted to a 0-to-10-point scale for scoring. For NPS, polyps on each side of the nose were graded on a categorical scale (0 = no polyps, 1 = small polyps in the middle meatus not reaching below the inferior border of the middle concha, 2 = polyps reaching below the lower border of the middle turbinate, 3 = large polyps reaching the lower border of the inferior turbinate or polyps medial to the middle concha, 4 = large polyps causing almost complete congestion/obstruction of the inferior meatus) for a total score of 0 to 8. Sinus CT scans were not performed at baseline nor during treatment to evaluate for sinus opacification. (7)

The co-primary endpoints were change from baseline to Week 52 in total endoscopic NPS (0 to 8 scale) as graded by independent blinded assessors and change from baseline in nasal obstruction VAS score (0 to 10 scale) during Weeks 49 to 52. The key secondary endpoint was the time to first nasal surgery (nasal polypectomy) up to Week 52 in this trial. Other secondary endpoints were change from baseline in loss of smell VAS score during Weeks 49 to 52, and proportion of patients requiring systemic steroids for nasal polyps up to Week 52. All VAS scores were collected daily by the patients and reported on a 0 to 10 scale (0 = none, 10 = as bad as you can imagine). Patients who received Nucala 100 mg had a statistically significant improvement (decrease) in bilateral NPS at Week 52 and nasal obstruction VAS score from Weeks 49 to 52 at the end of the 52-week treatment period. (7)

The key secondary endpoint was the time to first nasal surgery (nasal polypectomy) up to Week 52. The proportion of patients who had surgery was significantly reduced by 57% (hazard ratio: 0.43, 95% CI: 0.25, 0.76) in the group treated with Nucala 100 mg compared with the placebo group. By Week 52, 18 (9%) patients who received Nucala 100 mg had surgery compared with 46 (23%) patients in the placebo group. (7)

For patients who received Nucala 100 mg, statistically significant improvement was observed in loss of smell compared to placebo and improvements were also observed in the individual VAS symptom scores compared with patients in the placebo group in the 4-weeks prior to the end of the 52-week treatment period. (7)

Treatment with Nucala 100 mg significantly reduced the need for systemic steroids for nasal polyps vs. placebo up to Week 52 (odds ratio: 0.58, 95% CI: 0.36, 0.92). In patients who received Nucala 100 mg, 52 (25%) required ≥1 course of systemic steroids compared with 74 (37%) in the placebo group throughout the 52-week treatment period. (7)

In 289 (71%) patients with co-morbid asthma, pre-specified analyses showed improvements in the co-primary endpoints consistent with those seen in the overall population in the patients who received Nucala 100 mg compared with placebo. Additionally, based on a post-hoc analysis in these patients, there was a greater response from baseline at Week 52 in asthma control as measured by the Asthma Control Questionnaire (ACQ-5) for Nucala 100 mg compared with placebo (57% of the Nucala patients met the responder threshold reduction of ≥0.5, compared to 35% in the placebo group, with an odds ratio of 2.42 [95% CI 1.43, 4.11]). (7)

Summary of Evidence

For individuals aged 6 years and older with severe eosinophilic asthma, identified by blood eosinophil counts of at least 150 cells/µL at the start of treatment or 300 cells/µL in the past 12 months and with a positive history of exacerbations, treatment with mepolizumab consistently demonstrated benefits in the 3 pivotal trials in terms of reduced episodes of asthma exacerbation and reduced use of oral corticosteroids.

For individuals aged 12 years and older with hypereosinophilic syndrome (HES) and > 6 months without an identifiable non-hematologic HES or FIP1L1-PDGFRα kinase-positive HES including history of 2 or more HES flares, the evidence includes a randomized, double-blind, placebo-controlled, multicenter trial. This trial showed 50% fewer patients experienced a HES flare when treated with mepolizumab, compared to placebo, when added to standard of care treatment over the 32-week trial period.

For individuals aged 18 years and older with relapsing or refractory eosinophilic granulomatosis with polyangiitis (EGPA) (Churg-Strauss syndrome) the evidence includes a randomized, multicenter trial of 136 participants. The participants with EGPA resulted in significantly more weeks in remission and a higher proportion of participants in remission than did placebo.

For individuals aged 18 years and older with chronic rhinosinusitis with nasal polyps (CRSwNP), the evidence includes a randomized, double-blind, placebo-controlled, multicenter trial of 407 adult participants. Participants in this trial had a significant improvement in the size of nasal polyps, an improvement in nasal congestion, reduced need for nasal polypectomy, improvement in sense of smell, and a reduced need for systemic corticosteroids compared to placebo. For those individuals with co-morbid asthma, improvements were made in the co-primary endpoints consistent with those seen in the overall population in the patients who received Nucala compared with placebo.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	96372
HCPCS Codes	J2182, J3490, J3590

*Current Procedural Terminology (CPT®) ©2023 American Medical Association: Chicago, IL.

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Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision

Date	Description of Change
04/15/2025	Document updated. The following change was made to Coverage: Added "The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage of a formulation that cannot be self-administered is considered not medically necessary unless the patient has a physical or cognitive limitation that makes the utilization of a self-administered formulation unsafe or otherwise not feasible, as demonstrated by BOTH of the following: Inability to self-administer the medication, AND lack of caregiver or support system for assistance with administration of self-administered products." No new references added.
06/15/2024	Document updated with literature review. The following changes were made to Coverage: 1) Modified medical necessity criteria for Eosinophilic Asthma; 2) Modified NOTE 1; and 3) Modified medical necessity criteria for Chronic Rhinosinusitis with Nasal Polyps. Reference 1 and 6 added.
05/01/2023	Reviewed. No changes.
12/01/2022	Document updated with literature review. The following change was made to Coverage: Added a medically necessary coverage statement for the treatment of chronic rhinosinusitis with nasal polyps, and removed it from the experimental, investigational and/or unproven coverage statement. Reference 5 added, others updated and some removed.
06/15/2021	Document updated with literature review. The following addition was made to Coverage criteria for eosinophilic asthma: "Will not be used in combination with another antiasthmatic monoclonal antibody agent (e.g., omalizumab [Xolair], benralizumab [Fasenra], reslizumab [Cinqair])". No new references added.
12/01/2020	Document updated with literature review. The following change was made to Coverage: Added a medically necessary coverage statement for the

	treatment of hypereosinophilic syndrome and NOTES 3 and 4. Added reference 2 and others updated. Title changed from Mepolizumab (Nucala).
03/15/2020	Document updated with literature review. The following change was made to Coverage: For the medically necessary statement of treatment of severe eosinophilic asthma the age was changed from 12 years of age or older to 6 years of age or older. Reference 3 was added.
07/15/2018	Document updated with literature review. The following change(s) were made: Added conditional coverage for the treatment of relapsing or refractory eosinophilic granulomatosis with polyangiitis (EGPA) (Churg-Strauss syndrome) and it removed from the experimental, investigational and/or unproven coverage statement. References 1 and 4 were added.
04/15/2017	Reviewed. No changes.
04/01/2016	New medical document. Mepolizumab may be considered medically necessary for the treatment of severe eosinophilic asthma when the following criteria are met: 10 Individual is 12 years of age or older; AND 2) Patient meets definition of severe asthma as defined by the following: 12 months of treatment with high-dose inhaled corticosteroid (ICS) in combination with long-acting beta2-agonist (LABA) or leukotriene receptor antagonist [LTRA]/theophylline for the previous year or systemic corticosteroids for 50% or more of the previous year to prevent asthma from becoming uncontrolled or remaining uncontrolled; AND NOTE: Patients who do not meet the criteria for uncontrolled asthma, but whose asthma worsens on tapering off corticosteroids, will also meet this definition of severe asthma. For definition of uncontrolled asthma see description section; 3) History of 2 or more exacerbations requiring systemic glucocorticoids while being treated with fluticasone propionate 880µg or more or its equivalent in the last year; AND 4) Eosinophil count of the following (in the absence of other potential causes of eosinophilia, including hypereosinophilic syndromes, neoplastic disease, and known or suspected parasitic infection): 150 cells/µL or more in peripheral blood at screening or 300 cells/µL or more during the previous year; NOTE: 1 microliter (ul) is equal to 1 cubic millimeter (mm3). Mepolizumab is considered experimental, investigational and/or unproven when not meeting criteria as outlined above and for all other indications, including but not limited to: Eosinophilic chronic obstructive pulmonary disease, Eosinophilic esophagitis, Eosinophilic granulomatosis with polyangiitis (EGPA) (Churg-Strauss syndrome), Nasal polyposis and Hypereosinophilic syndromes (other than severe eosinophilic asthma).