Nucala® (mepolizumab)
(Subcutaneous)

Effective Date: 01/01/2020
Review Date: 12/18/2019, 12/20/2019, 1/29/2020, 9/9/2020, 11/2/2020, 3/18/2021, 01/05/2022, 1/05/2023, 12/07/23, 01/10/2024, 04/24/2024, 09/30/2025

Scope: Medicaid, Commercial, Medicare

I. Length of Authorization

Coverage is provided for six months and is eligible for renewal for 12 months.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- 100 mg/mL single dose vial for injection: 3 vials every 28 days
- 100 mg/mL single dose prefilled autoinjector or syringe for injection: 3 autoinjectors or syringes every 28 days
- 40mg/0.4ml single-dose prefilled syringe for injection: 1 syringe every 28 days

B. Max Units (per dose and over time) [HCPCS Unit]:

Severe Asthma with an eosinophilic phenotype

- 100 billable units every 28 days

EGPA

- 300 billable units every 28 days

Hypereosinophilic Syndrome

- 300 billable units every 28 days

CRSwNP & COPD

- 100 billable units every 28 days

III. Summary of evidence

Nucala (mepolizumab) is indicated in chronic rhinosinusitis with nasal polyps (CRSwNP) in adults aged 18 years and older who have an inadequate response to nasal corticosteroids, chronic obstructive pulmonary disease (COPD) in adults with an eosinophilic phenotype and inadequate disease control, eosinophilic granulomatosis with polyangiitis (EGPA) in adults, and hypereosinophilic syndrome (HES) in adults and pediatric patients aged 12 years and older. Clinical efficacy in asthma was demonstrated through three double-blind, randomized, placebo-controlled trials: DREAM (NCT01000506), MENSA (NCT01691521), and SIRIUS (NCT01691508). In all trials, mepolizumab was administered every four weeks as an add-on to background treatment. For CRSwNP,

a total of 407 adult patients were evaluated in a 52-week, randomized, double-blind, placebo-controlled, multicenter trial (NCT03085797). Patients received Nucala 100 mg or placebo subcutaneously every four weeks while continuing nasal corticosteroid therapy. Eligibility required a bilateral nasal polyp score (NPS) of at least 5 out of 8, with a minimum score of 2 in each nasal cavity. The co-primary endpoints were changes from baseline to Week 52 in total endoscopic NPS and nasal obstruction visual analog scale (VAS) score during Weeks 49 to 52. Nucala 100 mg resulted in statistically significant improvements in both endpoints compared to placebo. Efficacy in COPD was evaluated in two randomized, double-blind, placebo-controlled, multicenter trials: MATINEE (NCT04133909) and METREX (NCT02105948), enrolling a total of 1640 adults. Patients received Nucala 100 mg or placebo subcutaneously every four weeks for 52 to 104 weeks in MATINEE and 52 weeks in METREX. The primary endpoint in both trials was the annualized rate of moderate or severe exacerbations. Nucala demonstrated a statistically significant reduction in exacerbation rates compared to placebo when added to triple inhaled therapy. In EGPA, 136 adult patients participated in a 52-week, randomized, placebo-controlled, multicenter trial (NCT02020889). Patients received 300 mg of Nucala or placebo subcutaneously every four weeks while continuing stable daily oral corticosteroids. The primary efficacy measure was time in remission, defined as symptom-free status on a prednisone dose of 4 mg or less. Patients receiving Nucala achieved significantly greater accrued time in remission and a higher proportion of remission at Weeks 36 and 48 compared to placebo. 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 received 300 mg of Nucala or placebo subcutaneous once every 4 weeks while continuing their stable HES therapy. The trial compared the proportion of patients who experienced a HES flare or withdrew from the trial in the Nucala 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 Nucala (50% reduction). The most common adverse reactions reported in clinical trials included headache, injection site reactions, back pain, and fatigue.

IV. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

Medicare members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements.

Universal Criteria [1]

- Must not be used in combination with other anti-IgE, anti-IL4, anti-IL5, or IgG2 lambda monoclonal antibody agents (e.g., Dupixent, Fasenra, Nucala, Xolair, Tezspire); **AND**

Severe Asthma † [1-3,7,10]

- Member is at least 6 years of age; **AND**
- Member must have severe***** disease; **AND**
- Nucala is prescribed by, or in consultation with, a pulmonologist or allergist/immunologist; **AND**

- Member must have asthma with an eosinophilic phenotype defined as blood eosinophils ≥300 cells/μL within previous 12 months or ≥150 cells/μL within 6 weeks of dosing OR the member is dependent on systemic corticosteriods; **AND**
- Member is adherent to current treatment with both of the following medications at optimized doses:
    - Medium to high-dose inhaled corticosteroids; **AND**
    - An additional controller medication (e.g., long-acting beta agonist, long-acting muscarinic antagonists, leukotriene modifier), unless contraindicated or not tolerated; **AND**
- Will not be used for treatment acute bronchospasm or status asthmaticus; **AND**
- Member must have inadequate asthma control with two or more exacerbations in the previous year requiring additional medical treatment (e.g., daily oral corticosteroids for at least 3 days, emergency department or urgent care visits, or hospitalizations) in addition to the regular maintenance therapy defined above; **AND**
- Baseline measurement of at least one of the following for assessment of clinical status:
    - Use of systemic corticosteroids
    - Use of inhaled corticosteroids
    - Number of hospitalizations, ER visits, or unscheduled visits to healthcare provider due to condition
    - Forced expiratory volume in 1 second (FEV_1)

Eosinophilic Granulomatosis with Polyangiitis (EGPA)/Churg-Strauss Syndrome † Φ [1,5,6]

- Member is at least 18 years of age; **AND**
- Nucala is prescribed by, or in consultation with, a pulmonologist, rheumatologist or allergist/immunologist; **AND**
- Member has a confirmed diagnosis of EGPA§ (aka Churg-Strauss Syndrome); **AND**
- Member must have blood eosinophils ≥150 cells/μL within 6 weeks of dosing; **AND**
- Member has been on stable doses of concomitant oral corticosteroid therapy for at least 4 weeks (i.e., prednisone or prednisolone at a dose of 7.5 mg/day); **AND**
- Physician has assessed baseline disease severity utilizing an objective measure/tool (e.g., Birmingham Vasculitis Activity Score [BVAS], history of asthma symptoms and/or exacerbations, duration of remission, or rate of relapses, etc.)

Hypereosinophilic Syndrome (HES) † Φ [1,11]

- Member is at least 12 years of age; **AND**
- Member has been diagnosed with HES for at least 6 months prior to starting treatment; **AND**
- Member does NOT have non-hematologic secondary HES (e.g., drug hypersensitivity, parasitic helminth infection, HIV infection, non-hematologic malignancy) or FIP1L1-PDGFRα kinase-positive HES; **AND**

- Member has a history of 2 or more HES flares within the previous 12 months (e.g., documented HES-related worsening of clinical symptoms or blood eosinophil counts requiring an escalation in therapy); **AND**
- Member must have blood eosinophils ≥1000 cells/μL within 4 weeks of dosing; **AND**
- Used in combination with stable doses of at least one other HES therapy (e.g., oral corticosteroids, immunosuppressive agents, cytotoxic therapy, etc.)

Chronic Rhinosinusitis with Nasal Polyps (CRSwNP) † [1,15,16]

- Member is at least 18 years of age; **AND**
- Member has bilateral symptomatic sino-nasal polyposis with symptoms lasting at least 8 weeks; **AND**
- Member has failed on at least 8 weeks of intranasal corticosteroid therapy; **AND**
- Member has at least three (3) of the following indicators for biologic treatment:
    - Member has evidence of type 2 inflammation (e.g., tissue eosinophils ≥ 10/hpf, blood eosinophils ≥ 150 cells/μL, or total IgE ≥ 100 IU/mL)
    - Member has required ≥2 courses of systemic corticosteroids per year or >3 months of low dose corticosteroids, unless contraindicated
    - Disease significantly impairs the member's quality of life
    - Member has experienced significant loss of smell
    - Member has a comorbid diagnosis of asthma; **AND**
- Member does not have any of the following:
    - Antrochoanal polyps
    - Nasal septal deviation that would occlude at least one nostril
    - Disease with lack of signs of type 2 inflammation
    - Cystic fibrosis
    - Mucoceles; **AND**
- Other causes of nasal congestion/obstruction have been ruled out (e.g., acute sinusitis, nasal infection or upper respiratory infection, rhinitis medicamentosa, tumors, infections, granulomatosis, etc.); **AND**
- Physician has assessed baseline disease severity utilizing an objective measure/tool; **AND**
- Therapy will be used in combination with intranasal corticosteroids unless not able to tolerate or use is contraindicated

Chronic Obstructive Pulmonary Disease (COPD)

- Authorization may be granted for treatment of COPD in members when all of the following criteria are met:
    - Member is 18 years of age or older; **AND**

- Diagnosis has been confirmed by spirometry showing forced expiratory volume in one second (FEV1)/forced vital capacity (FVC) less than 0.7 post-bronchodilation; **AND**
- Member demonstrates classic signs or symptoms of COPD (e.g., dyspnea, wheezing, chest tightness, fatigue, activity limitation, cough with or without sputum production, chronic bronchitis); **AND**
- Member has an absolute blood eosinophil count of at least 150 cells per microliter prior to initiating therapy with the requested medication; **AND**
- Member has inadequately controlled COPD as demonstrated by experiencing either of the following in the last year:
  - At least two moderate exacerbations resulting in treatment with systemic glucocorticoids, antibiotics or both; OR
  - One or more severe exacerbation(s) requiring hospitalizations or an emergency medical care visit; **AND**
- Member meets either of the following:
  - Member is currently receiving maintenance inhaled triple therapy (i.e., inhaled corticosteroid [ICS], long-acting muscarinic antagonist [LAMA], and long-acting beta2-agonist [LABA]); OR
  - Member is currently receiving a LAMA and LABA, and has a contraindication to ICS ; **AND**
- Member will continue to use maintenance COPD treatments (e.g., ICS with LAMA and LABA, LAMA and LABA) in combination with the requested medication.

***Components of severity for classifying asthma as <u>severe</u> may include any of the following (not all):**

- Symptoms throughout the day
- Nighttime awakenings, often 7x/week
- SABA use for symptom control occurs several times per day
- Extremely limited normal activities
- Lung function (percent predicted FEV_1) <60%
- Exacerbations requiring oral systemic corticosteroids are generally more frequent and intense relative to moderate asthma

§Eosinophilic Granulomatosis Polyangiitis (EGPA) defined as all of the following:

- History or presence of asthma
- Blood eosinophil level > 10% or an absolute eosinophil count >1000 cells/mm^3
- Two or more of the following criteria:
  - Histopathologic evidence of eosinophilic vasculitis, perivascular eosinophilic infiltration or eosinophil rich granulomatous inflammation
  - Neuropathy
  - Pulmonary infiltrates

- Sinonasal abnormalities
- Cardiomyopathy
- Glomerulonephritis
- Alveolar hemorrhage
- Palpable purpura
- Antineutrophil Cytoplasmic Antibody (ANCA) positivity

† FDA-approved indication(s); **Φ** Orphan Drug

V. Renewal Criteria [1-3,5-7,10,11]

- Member continues to meet the universal and other indication-specific relevant criteria identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: parasitic (helminth) infection, herpes zoster infection, severe hypersensitivity reactions (e.g., anaphylaxis, angioedema, bronchospasm, hypotension, urticaria, rash, etc.); **AND**

Severe Asthma

- Improvement in asthma symptoms or asthma exacerbations as evidenced by decrease in one or more of the following:
  - Use of systemic corticosteroids
  - Two-fold or greater decrease in inhaled corticosteroid use for at least 3 days
  - Hospitalizations
  - ER visits
  - Unscheduled visits to healthcare provider; **OR**
- Improvement from baseline in forced expiratory volume in 1 second (FEV_1)

Eosinophilic Granulomatosis with Polyangiitis/Churg-Strauss Syndrome

- Disease response as indicated by improvement in signs and symptoms compared to baseline as evidenced by one or more of the following:
  - Member is in remission [defined as a Birmingham Vasculitis Activity Score (BVAS) score=0 and a prednisone/prednisolone daily dose of ≤ 7.5 mg]
  - Decrease in maintenance dose of systemic corticosteroids
  - Improvement in BVAS score compared to baseline
  - Improvement in asthma symptoms or asthma exacerbations
  - Improvement in duration of remission or decrease in the rate of relapses

Hypereosinophilic Syndrome (HES)

- Disease response as indicated by a decrease in HES flares from baseline *(**Note:** An HES flare is defined as worsening of clinical signs and symptoms of HES or increasing eosinophils (on at least 2 occasions), resulting in the need to increase oral corticosteroids or increase/add cytotoxic or immunosuppressive HES therapy).*

Chronic Rhinosinusitis with Nasal Polyps (CRSwNP) † [1,15]

- Disease response as indicated by improvement in signs and symptoms compared to baseline in one or more of the following: nasal/obstruction symptoms, improvement of sinus opacifications as assessed by CT-scans and/or an improvement on a disease activity scoring tool [e.g., nasal polyposis score (NPS), nasal congestion (NC) symptom severity score, sino-nasal outcome test-22 (SNOT-22), etc.]; **OR**
- Member had an improvement in at least one (1) of the following response criteria:
  - Reduction in nasal polyp size
  - Reduction in need for systemic corticosteroids
  - Improvement in quality of life
  - Improvement in sense of smell
  - Reduction of impact of comorbidities

Chronic Obstructive Pulmonary Disease (COPD)

- Member is 18 years of age or older
- Member has achieved or maintained a positive clinical response as evidenced by improvement in signs and symptoms of COPD (e.g., decrease in exacerbations, improvement in pre-bronchodilator FEV1) or stabilization of disease
- Member will continue to use maintenance COPD treatments (e.g., ICS with LAMA and LABA, LAMA and LABA) in combination with the requested medication.

VI. Dosage/Administration [1]

Indication	Dose
Severe Asthma with eosinophilic phenotype	Pediatric Members Aged 6 to 11 years (single dose vial only): 40 mg administered subcutaneously once every 4 weeks Adults and Adolescents Aged 12 years and older: 100 mg administered subcutaneously once every 4 weeks
Eosinophilic Granulomatosis with Polyangiitis/Churg-Strauss Syndrome	300 mg administered subcutaneously once every 4 weeks as 3 separate 100-mg injections. Administer each injection at least 2 inches apart.
Hypereosinophilic Syndrome (HES)	300 mg administered subcutaneously once every 4 weeks as 3 separate 100-mg injections. Administer each injection at least 2 inches apart.

Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)	100 mg administered subcutaneously once every 4 weeks.
Chronic Obstructive Pulmonary Disease (COPD)	100 mg administered subcutaneously once every 4 weeks.
***Note: Single dose vial must be prepared and administered by a healthcare professional, the auto-injector or prefilled syringe may be self-administered.*	

VII. Billing Code/Availability Information

HCPCS Code:

- J2182 - Injection, mepolizumab, 1 mg: 1 billable unit = 1 mg

NDC:

- 100 mg/mL single dose vial: 00173-0881-xx
- 100 mg/mL single dose prefilled autoinjector or syringe (cartons of 1): 00173-0892-xx

VIII. References

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Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
D72.1	Eosinophilia
J45.50	Severe persistent asthma, uncomplicated
J45.51	Severe persistent asthma with (acute) exacerbation
J45.52	Severe persistent asthma with status asthmaticus
J82.81	Eosinophilic pneumonia, NOS
J82.82	Acute eosinophilic pneumonia
J82.83	Eosinophilic asthma
J82.89	Other pulmonary eosinophilia, not elsewhere classified
M30.1	Polyarteritis with lung involvement [Churg-Strauss]

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outmember (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Policy Rationale:
Nucala was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Nucala according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For Medicare members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.