Nucala® (mepolizumab)
(Subcutaneous)

Document Number: EOCCO-0260

Last Review Date: 08/03/2021
Date of Origin: 12/04/2015
Dates Reviewed: 12/2015, 07/2016, 03/2017, 06/2017, 09/2017, 12/2017, 01/2018, 03/2018, 06/2018, 10/2018, 10/2019, 01/2020, 10/2020, 03/2021, 08/2021

I. Length of Authorization

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

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

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

- 100 billable units every 28 days

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

Universal Criteria [1]

- Must not be used in combination with another anti-IgE, anti-IL4, or anti-IL5 monoclonal antibody (e.g., benralizumab, omalizumab, reslizumab, dupilumab, etc.); **AND**

Severe Asthma † [1-3,7,10,12,13]

- Patient is at least 6 years of age; **AND**
- Patient must have severe* disease; **AND**

- Patient 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; **AND**
- Must be used for add-on maintenance treatment in patients regularly receiving BOTH of the following:
    - Medium to high-dose inhaled corticosteroids; **AND**
    - An additional controller medication (e.g., long-acting beta agonist, leukotriene modifiers, etc.); **AND**
- Will not be used for treatment of acute bronchospasm or status asthmaticus; **AND**
- Patient must have two or more exacerbations in the previous year requiring daily oral corticosteroids for at least 3 days (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]

- Patient is at least 18 years of age; **AND**
- Patient has a confirmed diagnosis of EGPA**§** (aka Churg-Strauss Syndrome); **AND**
- Patient must have blood eosinophils ≥150 cells/µL within 6 weeks of dosing; **AND**
- Patient 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]

- Patient is at least 12 years of age; **AND**
- Patient has been diagnosed with HES for at least 6 months prior to starting treatment; **AND**
- Patient 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**

- Patient 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**
- Patient 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]

- Patient is at least 18 years of age; **AND**
- Patient has bilateral symptomatic sino-nasal polyposis with symptoms lasting at least 8 weeks; **AND**
- Patient has failed on at least 8 weeks of intranasal corticosteroid therapy; **AND**
- Patient has at least four (4) of the following indicators for biologic treatment *[Note: Patients with a history of sino-nasal surgery are only required to have at least three (3) of the indicators]:*
    - Patient has evidence of type 2 inflammation (i.e., biological biomarkers indicating immune dysregulation and epithelial barrier dysfunction)
    - Patient has required two or more short courses of systemic corticosteroids within the previous year
    - Disease significantly impairs the patient's quality of life
    - Patient has experienced significant loss of smell
    - Patient has a comorbid diagnosis of asthma; **AND**
- Patient 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 is contraindicated

*Components of severity for classifying asthma as severe may include any of the following (not all inclusive):[2]
• 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:[6]
• 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

IV. Renewal Criteria [1-3,5-7,10,11,15]

- Patient 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, 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 in one or more of the following:
  - Patient 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**
- Patient 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

V. Dosage/Administration [1]

Indication	Dose
Severe Asthma with eosinophilic phenotype	Pediatric Patients 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.
Note: Single dose vial must be prepared and administered by a healthcare professional, the auto-injector or prefilled syringe may be self-administered.	

VI. Billing Code/Availability Information

HCPCS Code:

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

NDC:

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

VII. References

1. Nucala [package insert]. Philadelphia, PA; GlaxoSmithKline LLC; July 2021. Accessed July 2021.
2. National Asthma Education and Prevention Program (NAEPP). Guidelines for the diagnosis and management of asthma. Expert Panel Report 3. Bethesda, MD: National Institutes of Health (NIH), National Heart, Lung, and Blood Institute (NHLBI); August 2007.
3. Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention. 2019 Update. Available from: http://www.ginasthma.org. Accessed September 2020.
4. Wechsler ME, Akuthota P, Jayne D, et al. Mepolizumab or Placebo for Eosinophilic Granulomatosis with Polyangiitis. N Engl J Med. 2017 May 18;376(20):1921-1932. doi: 10.1056/NEJMoa1702079.
5. Hellmich B, Flossmann O, Gross WL, et al. EULAR recommendations for conducting clinical studies and/or clinical trials in systemic vasculitis: focus on antineutrophil cytoplasm antibody-associated vasculitis. Ann Rheum Dis 2007; 66: 605-17.
6. Masi AT, Hunder GG, Lie JT; Michel BA, et al. The American College of Rheumatology 1990 criteria for the classification of Churg-Strauss syndrome (allergic granulomatosis and angiitis). Arthritis Rheum. 1990; 33(8):1094-100 (ISSN: 0004-3591).
7. Chung KF, Wenzel SE, Brozek JL, et al. International ERS/ATS Guidelines on Definition, Evaluation, and Treatment of Severe Asthma. Eur Respir J 2014; 43: 343-373.
8. Yates M, Watts RA, Bajema IM, et al. EULAR/ERA-EDTA recommendations for the management of ANCA-associated vasculitis. Ann Rheum Dis. 2016 Sep;75(9):1583-94. doi: 10.1136/annrheumdis-2016-209133.

9. Groh M, Panoux C, Baldini C, et al. Eosinophilic granulomatosis with polyangiitis (Churg–Strauss) (EGPA) Consensus Task Force recommendations for evaluation and management. European Journal of Internal Medicine 26 (2015) 545–553.
10. Holguin F, Cardet JC, Chung KF, et al. Management of severe asthma: a European Respiratory Society/American Thoracic Society guideline. Eur Respir J 2020; 55: 1900588 [https://doi.org/10.1183/13993003.00588-2019]
11. Roufosse F, Kahn JE, Rothenberg ME, et al. Efficacy and safety of mepolizumab in hypereosinophilic syndrome: a Phase III, randomized, placebo-controlled trial. Journal of Allergy and Clinical Immunology (2020), doi: https://doi.org/10.1016/j.jaci.2020.08.037.
12. National Asthma Education and Prevention Program (NAEPP). 2020 Focused Updates to the Asthma Management Guidelines: A Report from the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group. Bethesda, MD: National Institutes of Health (NIH), National Heart, Lung, and Blood Institute (NHLBI); December 2020.
13. Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention. 2021 Update. Available from: http://www.ginasthma.org. Accessed June 2021.
14. Han JK, Bachert C, Fokkens W, et al; SYNAPSE study investigators. Mepolizumab for chronic rhinosinusitis with nasal polyps (SYNAPSE): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Respir Med. 2021 Apr 16:S2213-2600(21)00097-7. doi: 10.1016/S2213-2600(21)00097-7.
15. Fokkens WJ, Lund V, Bachert C, et al. EUFOREA consensus on biologics for CRSwNP with or without asthma. *Allergy.* 2019;74:2312–2319. DOI: 10.1111/all.13875.
16. Gandhi NA, Bennett BL, Graham NMH, et al. Targeting key proximal drivers of type 2 inflammation in disease. Nat Rev Drug Discov. 2016;15(1):35-50.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
D72.110	Idiopathic hypereosinophilic syndrome [IHES]
D72.111	Lymphocytic Variant Hypereosinophilic Syndrome [LHES]
D72.119	Hypereosinophilic syndrome [HES], unspecified
J33.0	Polyp of nasal cavity
J33.1	Polypoid sinus degeneration
J33.8	Other polyp of sinus
J33.9	Nasal polyp, unspecified
J45.50	Severe persistent asthma, uncomplicated
J82.81	Eosinophilic pneumonia, NOS
J82.82	Acute eosinophilic pneumonia
J82.83	Eosinophilic asthma

ICD-10	ICD-10 Description
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 outpatient (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.
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