

## **Clinical Policy: Mepolizumab (Nucala)**

Reference Number: CP.PHAR.200

Effective Date: 04.01.16

Last Review Date: 02.19

Line of Business: Commercial, HIM, Medicaid

[Coding Implications](#)  
[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

### **Description**

Mepolizumab (Nucala<sup>®</sup>) is an interleukin-5 antagonist monoclonal antibody (IgG1 kappa).

### **FDA Approved Indication(s)**

Nucala is indicated for:

- Add-on maintenance treatment of patients with severe asthma aged 12 years and older, and with an eosinophilic phenotype.
- Treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA).

Limitation(s) of use: Nucala is not indicated for the relief of acute bronchospasm or status asthmaticus.

### **Policy/Criteria**

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of health plans affiliated with Centene Corporation<sup>®</sup> that Nucala is **medically necessary** when the following criteria are met:

#### **I. Initial Approval Criteria**

##### **A. Severe Asthma (must meet all):**

1. Diagnosis of asthma;
2. Member has an absolute blood eosinophil count  $\geq 150$  cells/mcL within the past 3 months;
3. Prescribed by or in consultation with a pulmonologist, immunologist, or allergist;
4. Age  $\geq 12$  years;
5. Member has experienced  $\geq 2$  exacerbations with in the last 12 months, requiring any of the following despite adherent use of controller therapy (i.e., medium- to high-dose inhaled corticosteroid (ICS) plus either a long acting beta-2 agonist (LABA) or leukotriene modifier (LTRA) if LABA contraindication/intolerance):
  - a. Oral/systemic corticosteroid treatment (or increase in dose if already on oral corticosteroid);
  - b. Urgent care visit or hospital admission;
  - c. Intubation;
6. Nucala is prescribed concomitantly with an ICS plus either a LABA or LTRA;
7. Dose does not exceed 100 mg every 4 weeks.

**Approval duration: 6 months**

**B. Eosinophilic Granulomatosis with Polyangiitis (Churg-Strauss) (must meet all):**

1. Diagnosis of EGPA (Churg-Strauss);
2. Member has an absolute blood eosinophil count  $\geq 150$  cells/mcL within the last 3 months;
3. Prescribed by or in consultation with a pulmonologist, rheumatologist, immunologist, or nephrologist;
4. Age  $\geq 18$  years;
5. Failure of a 3-month trial of a glucocorticoid (*see Appendix B*), unless contraindicated or clinically significant adverse events are experienced;
6. Dose does not exceed 300 mg every 4 weeks.

**Approval duration: 6 months**

**C. Other diagnoses/indications**

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**II. Continued Therapy**

**A. Severe Asthma (must meet all):**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Demonstrated adherence to asthma controller therapy that includes an ICS plus either an LABA or LTRA;
3. Member is responding positively to therapy (examples may include but are not limited to a reduction in exacerbations or corticosteroid dose, improvement in forced expiratory volume over one second since baseline; reduction in the use of rescue therapy);
4. If request is for a dose increase, new dose does not exceed 100 mg every 4 weeks.

**Approval duration:**

**Medicaid/HIM** – 12 months

**Commercial** – 6 months or member's renewal period, whichever is longer

**B. Eosinophilic Granulomatosis with Polyangiitis (Churg-Strauss) (must meet all):**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 300 mg every 4 weeks.

**Approval duration:**

**Medicaid/HIM** – 12 months

**Commercial** – 6 months or member's renewal period, whichever is longer

**C. Other diagnoses/indications (must meet 1 or 2):**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

- Approval duration: Duration of request or 6 months (whichever is less); or**
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**III. Diagnoses/Indications for which coverage is NOT authorized:**

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents;
- B. Acute bronchospasm or status asthmaticus.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

EGPA: eosinophilic granulomatosis with polyangiitis  
 FDA: Food and Drug Administration  
 GINA: Global Initiative for Asthma

ICS: inhaled corticosteroid  
 LABA: Long-acting beta-agonist  
 LTRA: leukotriene modifier

*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.*

| Drug Name  | Dosing Regimen   | Dose Limit/<br>Maximum Dose |
|--|--|-----------------------------|
| <b>Asthma - ICS (medium – high dose)</b>           |  |                             |
| Qvar <sup>®</sup> (beclomethasone)                 | > 200 mcg/day<br>40 mcg, 80 mcg per actuation<br>1-4 actuations BID  | 4 actuations BID            |
| budesonide (Pulmicort <sup>®</sup> )               | > 400 mcg/day<br>90 mcg, 180 mcg per actuation<br>2-4 actuations BID | 2 actuations BID            |
| Alvesco <sup>®</sup> (ciclesonide)                 | > 160 mcg/day<br>80 mcg, 160 mcg per actuation<br>1-2 actuations BID | 2 actuations BID            |
| Aerospan <sup>®</sup> (flunisolide)                | > 320 mcg/day<br>80 mcg per actuation<br>2-4 actuations BID          | 2 actuations BID            |
| Flovent <sup>®</sup> (fluticasone propionate)      | > 250 mcg/day<br>44-250 mcg per actuation<br>2-4 actuations BID      | 2 actuations BID            |
| Arnuity Ellipta <sup>®</sup> (fluticasone furoate) | 200 mcg/day<br>100 mcg, 200 mcg per actuation<br>1 actuation QD      | 1 actuation QD              |
| Asmanex <sup>®</sup> (mometasone)                  | >220 mcg/day   | 2 inhalations BID           |

| <b>Drug Name</b>                                   | <b>Dosing Regimen</b>   | <b>Dose Limit/<br/>Maximum Dose</b> |
|--|---|-------------------------------------|
|  | HFA: 100 mcg, 200 mcg per actuation<br>Twisthaler: 110 mcg, 220 mcg per actuation<br>1-2 actuations QD to BID |                                     |
| <b>Asthma - LABA</b>                               |   |                                     |
| Serevent® (salmeterol)                             | 50 mcg per dose<br>1 inhalation BID   | 1 inhalation BID                    |
| <b>Asthma - Combination products (ICS + LABA)</b>  |   |                                     |
| Dulera® (mometasone/formoterol)                    | 100/5 mcg, 200/5 mcg per actuation<br>2 actuations BID  | 4 actuations per day                |
| Breo Ellipta® (fluticasone/vilanterol)             | 100/25 mcg, 200/25 mcg per actuation<br>1 actuation QD  | 1 actuation QD                      |
| Advair® (fluticasone/salmeterol)                   | 100/50 mcg, 250/50 mcg, 500/50 mcg per actuation<br>1 actuation BID   | 1 actuation BID                     |
| Fluticasone/salmeterol (Airduo RespiClick®)        | 55/13 mcg, 113/14 mcg, 232/14 mcg per actuation<br>1 actuation BID  | 1 actuation BID                     |
| Symbicort® (budesonide/formoterol)                 | 80 mcg/4.5 mcg; 160 mcg/4.5 mcg per actuation<br>1-2 actuations BID   | 2 actuations BID                    |
| <b>Asthma - LTRA</b>                               |   |                                     |
| Montelukast (Singulair®)                           | 4 to 10 mg PO QD  | 10 mg per day                       |
| Zafirlukast (Accolate®)                            | 10 to 20 mg PO BID  | 40 mg per day                       |
| zileuton ER (Zyflo® CR)                            | 1200 mg PO BID  | 2400 mg per day                     |
| Zyflo® (zileuton)                                  | 1200 mg PO BID  | 2400 mg per day                     |
| <b>Oral glucocorticoids</b>                        |   |                                     |
| Dexamethasone (Decadron) for asthma                | 0.75 to 9 mg/day PO in 2 to 4 divided doses   | Varies                              |
| Methylprednisolone (Medrol) for asthma             | 40 to 80 mg PO in 1 to 2 divided doses  | Varies                              |
| prednisolone (Millipred®, Orapred ODT®) for asthma | 40 to 80 mg PO in 1 to 2 divided doses  | Varies                              |
| prednisone (Deltasone®) for asthma                 | 40 to 80 mg PO in 1 to 2 divided doses  | Varies                              |
| Methylprednisolone (Medrol) for EGPA               | 6.0 mg/day to 0.8 mg/kg/day   | Varies                              |

| Drug Name                       | Dosing Regimen               | Dose Limit/<br>Maximum Dose |
|---------------------------------|------------------------------|-----------------------------|
| Prednisone (Deltasone) for EGPA | 7.5 mg/day to<br>1 mg/kg/day | Varies                      |

*Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) when the drug is available by both brand and generic.*

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s): hypersensitivity
- Boxed warning(s): none reported

*Appendix D: General Information*

- Nucala is not indicated for relief of acute bronchospasm or status asthmaticus.
- The pivotal trials defined severe asthma as two or more exacerbations of asthma despite regular use of high-dose inhaled corticosteroids plus an additional controller with or without oral corticosteroids. Clinically significant exacerbation was defined as a worsening of asthma leading to the doubling (or more) of the existing maintenance dose of oral glucocorticoids for three or more days or hospital admission or an emergency department visit for asthma treatment.
- Controller medications are: inhaled glucocorticoids (Flovent, Pulmicort, Qvar, Asmanex), long-acting beta-agonists (LABAs) such as salmeterol, formoterol, or vilanterol, and antileukotriene agents (montelukast [Singulair<sup>®</sup>], zafirlukast [Accolate<sup>®</sup>] or Zyflo<sup>®</sup> [zileuton]). Theophylline is also a controller agent; however, it is not as efficacious as LABAs.
- Patients could potentially meet criteria for both Xolair and Nucala. The combination has not been studied. Approximately 30% of patients in the MENSA study also were candidates for therapy with Xolair.
- In the pivotal trial for treatment of EGPA, patients with a baseline blood eosinophil count < 150 cells/mcL did not have a statistically significant improvement in the primary endpoint, total accrued weeks of remission, when mepolizumab was compared to placebo (odds ratio, 0.95; 95% CI 0.28 to 3.24). Total number of weeks of remission was significantly greater in patients with a baseline eosinophil count ≥ 150 cells/mcL (odds ratio, 26.10; 95% CI 7.02 to 97.02).
- Standard of care for EGPA is oral glucocorticoids. Induction therapy of prednisone 1 mg/kg/day is recommended for 2-3 weeks followed by gradual tapering to the minimal effective dose. Patients with stable doses of prednisone ≤ 7.5 mg/day are considered to be in remission, as defined by the European League Against Rheumatism (EULAR) and in the pivotal trial. The EGPA Consensus Task Force recommends that patients who are unable to taper prednisone to < 7.5 mg/day after 3-4 months of therapy should be considered for additional immunosuppressant therapy.
- Positive response to therapy for asthma may include reduction in exacerbations or corticosteroid dose, improvement in forced expiratory volume over one second since baseline, or reduction in the use of rescue therapy.
- Positive response to therapy for EGPA is defined as a reduction of relapses or reduction in glucocorticoid dose. EULAR defines a relapse as the appearance of new or worsening clinical manifestations, not including asthma and/or ear, nose, and throat.

- Lab results for blood eosinophil counts can be converted into cells/mcL using the following unit conversion calculator: <https://www.gsksource.com/pharma/content/microsites/nucala-eos-calc/index.html>

## V. Dosage and Administration

| Indication    | Dosing Regimen          | Maximum Dose         |
|---------------|-------------------------|----------------------|
| Severe asthma | 100 mg SC every 4 weeks | 100 mg every 4 weeks |
| EGPA          | 300 mg SC every 4 weeks | 300 mg every 4 weeks |

## VI. Product Availability

- Single-dose vial: 100 mg of lyophilized powder for reconstitution
- Single-dose prefilled glass syringe with needle for injection: 100 mg/mL
- Single-dose prefilled autoinjector with needle for injection: 100 mg/mL

## VII. References

1. Nucala Prescribing Information. Philadelphia, PA: GlaxoSmithKline LLC; June 2019. Available at: <http://www.nucala.com>. Accessed July 7, 2019.
2. National Asthma Education and Prevention Program: Expert panel report III: Guidelines for the diagnosis and management of asthma. Bethesda, MD: National Heart, Lung, and Blood Institute, 2007. (NIH publication no. 08-4051). Available at <http://www.nhlbi.nih.gov/health-pro/guidelines/current/asthma-guidelines>. Accessed November 2017.
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4. Ortega HG, Liu MC, Pavord ID, et al. Mepolizumab treatment in patients with severe eosinophilic asthma. *N Engl J Med* 2014; 371:1198-207.
5. Bel EH, Wenzel SE, Thompson PH, et al. Oral glucocorticoid-sparing effect of mepolizumab in eosinophilic asthma. *New Engl J Med* 2014; 371:1189-97.
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7. 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.
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9. Hellmich B, Flossmann O, Gross WL, et al. EULAR recommendations for conducting clinical studies and/or clinical trials in systemic vasculitis: focus on anti-neutrophil cytoplasm antibody-associated vasculitis. *Ann Rheum Dis*. 2007 May;66(5):605-17.
10. Mukhtyar C, Guillevin L, Cid MC, et al. EULAR recommendations for the management of primary small and medium vessel vasculitis. *Ann Rheum Dis*. 2009;68(3):310-7.
11. Global Initiative for Asthma: Global strategy for asthma management and prevention (2018 update). Available at: <https://ginasthma.org/2018-gina-report-global-strategy-for-asthma-management-and-prevention/>. Accessed November 13, 2018.

**Coding Implications**

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

| HCPCS Codes | Description                  |
|-------------|------------------------------|
| J2182       | Injection, mepolizumab, 1 mg |

| Reviews, Revisions, and Approvals   | Date     | P&T Approval Date |
|---|----------|-------------------|
| Policy developed.   | 03.16    | 04.16             |
| Controller trial requirements are edited in the initial and renewal criteria and a smoking cessation line item is added. Efficacy statement is added to renewal criteria. Approval durations changed to 6 and 12 months.  | 03.17    | 04.17             |
| Changed temporary HCPCS code C9473 to permanent code J2182  | 08.17    | 02.18             |
| 1Q18 annual review <ul style="list-style-type: none"> <li>• Combined Medicaid and Commercial policies.</li> <li>• Removed smoking cessation program requirements from existing Medicaid policy as this cannot be enforced. - Added “Acute bronchospasm or status asthmaticus” to section III as indications for which coverage is not authorized per PI.</li> <li>• References reviewed and updated.</li> </ul> | 11.06.17 | 02.18             |
| Criteria added for new FDA indication: treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EPGA).   | 01.23.18 | 05.18             |
| Link to blood eosinophil unit conversion calculator added to Appendix C.  | 03.21.18 |                   |
| 1Q 2019 annual review: modified ICS requirement to include medium dose ICS per GINA 2018 recommendations; added option for immunologist prescribing for asthma; modified initial approval duration to 6 months for all lines of business; references reviewed and updated.  | 10.11.18 | 02.19             |
| Added HIM line of business due to addition of agent(s) to the HIM formulary with PA   | 03.14.19 |                   |
| RT4: added new 100 mg/mL self-administered PFS and auto-injector formulations.  | 07.07.19 |                   |

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and

accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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**Note:**

**For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

**For Health Insurance Marketplace members**, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the non-formulary policy; HIM.PA.103.

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