Clinical Policy: Mepolizumab (Nucala)
Reference Number: CP.PHAR.200
Effective Date: 05.01.16
Last Review Date: 02.21
Line of Business: Commercial, HIM, Medicaid

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Mepolizumab (Nucala®) 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 6 years and older, and with an eosinophilic phenotype.
• Treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA).
• Treatment of adult and pediatric patients aged 12 years and older with hypereosinophilic syndrome (HES) for ≥ 6 months without an identifiable non-hematologic secondary cause.

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® 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 ≥ 150 cells/mcL within the past 3 months;
      3. Prescribed by or in consultation with a pulmonologist, immunologist, or allergist;
      4. Age ≥ 6 years;
      5. Member has experienced ≥ 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 concurrently with an ICS plus either a LABA or LTRA;
7. Nucala is not prescribed concurrently with Cinqair®, Fasenra®, Dupixent®, or Xolair®;

8. Dose does not exceed (a or b):
   a. Age 6 to 11 years: 40 mg every 4 weeks;
   b. Age ≥ 12 years: 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 ≥ 150 cells/mcL within the past 3 months;
3. Prescribed by or in consultation with a pulmonologist, rheumatologist, immunologist, or nephrologist;
4. Age ≥ 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. Nucala is not prescribed concurrently with Cinqair, Fasenra, Dupixent, or Xolair;
7. Dose does not exceed 300 mg every 4 weeks.

**Approval duration: 6 months**

### C. Hypereosinophilic Syndrome (must meet all):
1. Diagnosis of HES with all of the following characteristics (a, b, and c):
   a. FIP1L1-PDGFRA negative;
   b. Does not have a non-hematologic secondary cause (e.g., drug sensitivity, parasite helminth infection, HIV infection, non-hematological malignancy);
   c. Uncontrolled, defined as a history of ≥ 2 flares (*see Appendix D*) within the past 12 months;
2. Prescribed by or in consultation with a hematologist, dermatologist, or immunologist;
3. Age ≥ 12 years;
4. Member has a blood eosinophil count ≥ 1,000 cells/mcL within the past 3 months;
5. Failure of a 2-month trial of a corticosteroid (*see Appendix B*) within one of the following time frames (a or b), unless contraindicated or clinically significant adverse events are experienced:
   a. Within the last 6 months;
   b. Within the last year if the member’s current HES baseline therapy includes interferon-alfa, cyclosporine, azathioprine, hydroxyurea, or imatinib;
6. Nucala is prescribed concurrently with baseline HES therapy (e.g., oral corticosteroids, immunosuppressive therapy);
7. Nucala is not prescribed concurrently with Cinqair, Fasenra, Dupixent, or Xolair;
8. Dose does not exceed 300 mg every 4 weeks.

**Approval duration: 6 months**

### D. 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...
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: reduction in exacerbations or corticosteroid dose, improvement in forced expiratory volume over one second since baseline, reduction in the use of rescue therapy);
   4. Nucala is not prescribed concurrently with Cinqair, Fasenra, Dupixent, or Xolair;
   5. If request is for a dose increase, new dose does not exceed (a or b):
      a. Age 6 to 11 years: 40 mg every 4 weeks;
      b. Age ≥ 12 years: 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 (examples may include but are not limited to: reduction of relapses or reduction in glucocorticoid dose);
   3. Nucala is not prescribed concurrently with Cinqair, Fasenra, Dupixent, or Xolair;
   4. 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. **Hypereosinophilic Syndrome** (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 with reduction in flares from baseline or reduction in maintenance HES therapy dose from baseline (*see Appendix D*);
   3. Nucala is prescribed concurrently with baseline HES therapy (e.g., oral corticosteroids, immunosuppressive therapy);
   4. Nucala is not prescribed concurrently with Cinqair, Fasenra, Dupixent, or Xolair;
   5. 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
D. 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.PA.154 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.PA.154 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
- FIP1L1-PDGFRα: Fip1-like1-platelet-derived growth factor receptor alpha
- GINA: Global Initiative for Asthma
- HES: hypereosinophilic syndrome
- 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.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Asthma - ICS (medium – high dose)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Qvar® (beclomethasone)</td>
<td>&gt; 200 mcg/day 40 mcg, 80 mcg per actuation 1-4 actuations BID</td>
<td>4 actuations BID</td>
</tr>
<tr>
<td>budesonide (Pulmicort®)</td>
<td>&gt; 400 mcg/day 90 mcg, 180 mcg per actuation 2-4 actuations BID</td>
<td>2 actuations BID</td>
</tr>
<tr>
<td>Alvesco® (ciclesonide)</td>
<td>&gt; 160 mcg/day 80 mcg, 160 mcg per actuation 1-2 actuations BID</td>
<td>2 actuations BID</td>
</tr>
<tr>
<td>Aerospan® (flunisolide)</td>
<td>&gt; 320 mcg/day 80 mcg per actuation 2-4 actuations BID</td>
<td>2 actuations BID</td>
</tr>
<tr>
<td>Flovent® (fluticasone propionate)</td>
<td>&gt; 250 mcg/day 44-250 mcg per actuation 2-4 actuations BID</td>
<td>2 actuations BID</td>
</tr>
<tr>
<td>Drug Name</td>
<td>Dosing Regimen</td>
<td>Dose Limit/Maximum Dose</td>
</tr>
<tr>
<td>---------------------------</td>
<td>-------------------------------------------------------------------------------</td>
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</tr>
<tr>
<td>Arnuity Ellipta® (fluticasone furoate)</td>
<td>200 mcg/day 100 mcg, 200 mcg per actuation 1 actuation QD</td>
<td>1 actuation QD</td>
</tr>
<tr>
<td>Asmanex® (mometasone)</td>
<td>&gt;220 mcg/day HFA: 100 mcg, 200 mcg per actuation Twistrhaler: 110 mcg, 220 mcg per actuation 1-2 actuations QD to BID</td>
<td>2 inhalations BID</td>
</tr>
<tr>
<td><strong>Asthma - LABA</strong></td>
<td></td>
<td></td>
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<tr>
<td>Serevent® (salmeterol)</td>
<td>50 mcg per dose 1 inhalation BID</td>
<td>1 inhalation BID</td>
</tr>
<tr>
<td><strong>Asthma - Combination Products (ICS + LABA)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dulera® (mometasone/ formoterol)</td>
<td>100/5 mcg, 200/5 mcg per actuation 2 actuations BID</td>
<td>4 actuations per day</td>
</tr>
<tr>
<td>Breo Ellipta® (fluticasone/ vilanterol)</td>
<td>100/25 mcg, 200/25 mcg per actuation 1 actuation QD</td>
<td>1 actuation QD</td>
</tr>
<tr>
<td>Advair® (fluticasone/ salmeterol)</td>
<td>100/50 mcg, 250/50 mcg, 500/50 mcg per actuation 1 actuation BID</td>
<td>1 actuation BID</td>
</tr>
<tr>
<td>Fluticasone/salmeterol (Airduo RespiClick®)</td>
<td>55/13 mcg, 113/14 mcg, 232/14 mcg per actuation 1 actuation BID</td>
<td>1 actuation BID</td>
</tr>
<tr>
<td>Symbicort® (budesonide/ formoterol)</td>
<td>80 mcg/4.5 mcg; 160 mcg/4.5 mcg per actuation 1-2 actuations BID</td>
<td>2 actuations BID</td>
</tr>
<tr>
<td><strong>Asthma - LTRA</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>montelukast (Singulair®)</td>
<td>4 to 10 mg PO QD</td>
<td>10 mg per day</td>
</tr>
<tr>
<td>zafirlukast (Accolate®)</td>
<td>10 to 20 mg PO BID</td>
<td>40 mg per day</td>
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<tr>
<td>zileuton ER (Zyflo® CR)</td>
<td>1,200 mg PO BID</td>
<td>2,400 mg per day</td>
</tr>
<tr>
<td>Zyflo® (zileuton)</td>
<td>1,200 mg PO BID</td>
<td>2,400 mg per day</td>
</tr>
<tr>
<td><strong>Oral Glucocorticoids</strong></td>
<td></td>
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<tr>
<td>dexamethasone (Decadron) for asthma</td>
<td>0.75 to 9 mg/day PO in 2 to 4 divided doses</td>
<td>Varies</td>
</tr>
<tr>
<td>methylprednisolone (Medrol) for asthma</td>
<td>40 to 80 mg PO in 1 to 2 divided doses</td>
<td>Varies</td>
</tr>
<tr>
<td>prednisolone (Millipred®, Orapred ODT®) for asthma</td>
<td>40 to 80 mg PO in 1 to 2 divided doses</td>
<td>Varies</td>
</tr>
<tr>
<td>prednisone (Deltasone®) for asthma</td>
<td>40 to 80 mg PO in 1 to 2 divided doses</td>
<td>Varies</td>
</tr>
<tr>
<td>Drug Name</td>
<td>Dosing Regimen</td>
<td>Dose Limit/Maximum Dose</td>
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</tr>
<tr>
<td>methylprednisolone (Medrol) for EGPA</td>
<td>6.0 mg/day to 0.8 mg/kg/day</td>
<td>Varies</td>
</tr>
<tr>
<td>prednisone (Deltasone) for EGPA</td>
<td>7.5 mg/day to 1 mg/kg/day</td>
<td>Varies</td>
</tr>
<tr>
<td>HES</td>
<td></td>
<td></td>
</tr>
<tr>
<td>oral corticosteroids: prednisolone, prednisone (off-label)</td>
<td>0.5 – 1 mg/kg/day</td>
<td>Varies</td>
</tr>
<tr>
<td>interferon alfa-2b (Intron-A®) (off-label)</td>
<td>1 – 6.25 million IU subcutaneously daily</td>
<td>20 million IU/m²/day</td>
</tr>
<tr>
<td>imatinib (Gleevec®)</td>
<td>100 – 400 mg PO QD</td>
<td>400 mg/day</td>
</tr>
<tr>
<td>cyclosporine (off-label)</td>
<td>150 – 500 mg PO QD</td>
<td>Varies</td>
</tr>
<tr>
<td>azathioprine (off-label)</td>
<td>1 – 3 mg/kg PO QD</td>
<td>Varies</td>
</tr>
<tr>
<td>hydroxyurea (off-label)</td>
<td>0.5 – 3 gm PO QD with or without corticosteroid</td>
<td>80 mg/day</td>
</tr>
</tbody>
</table>

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) 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
- 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.
- The 2019 Global Initiative for Asthma (GINA) guidelines for difficult-to-treat and severe asthma recommend Nucala be considered as adjunct therapy for patients 18 years of age and older with exacerbations or poor symptom control despite taking at least high dose ICS/LABA and who have allergic or eosinophilic biomarkers or need maintenance oral corticosteroids. Per 2020 GINA guidelines, Nucala may also be considered if the patient is uncontrolled on Step 4 treatment (medium dose ICS/LABA).
- Patients could potentially meet asthma criteria for both Xolair and Nucala, though data is insufficient to support combination use of multiple asthma biologics. 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.

- EULAR defines an EGPA 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

- Flares defined as a worsening of HES related clinical symptoms (e.g., pain, pruritus, skin lesions, nasal congestion, polyposis, dysphagia, or fatigue). An increase in blood eosinophil count requiring an escalation in therapy or above the predefined threshold level. An increase in maintenance oral corticosteroid dose by greater than or equal to 10 mg for 5 days or increase in/addition of any cytotoxic and/or immunosuppressive HES therapy.

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe asthma</td>
<td>Age 6 to 11 years: 40 mg SC every 4 weeks&lt;br&gt;Age ≥ 12 years: 100 mg SC every 4 weeks</td>
<td>100 mg every 4 weeks</td>
</tr>
<tr>
<td>EGPA, HES</td>
<td>300 mg SC every 4 weeks</td>
<td>300 mg every 4 weeks</td>
</tr>
</tbody>
</table>

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


**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.

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>J2182</td>
<td>Injection, mepolizumab, 1 mg</td>
</tr>
</tbody>
</table>

**Reviews, Revisions, and Approvals**

<table>
<thead>
<tr>
<th></th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>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.</td>
<td>03.17</td>
<td>04.17</td>
</tr>
<tr>
<td>Changed temporary HCPCS code C9473 to permanent code J2182</td>
<td>08.17</td>
<td>02.18</td>
</tr>
<tr>
<td>1Q18 annual review &lt;ul&gt;&lt;li&gt;Combined Medicaid and Commercial policies.&lt;/li&gt;&lt;li&gt;Removed smoking cessation program requirements from existing Medicaid policy as this cannot be enforced. - Added “Acute&lt;/li&gt;&lt;/ul&gt;</td>
<td>11.06.17</td>
<td>02.18</td>
</tr>
</tbody>
</table>
Reviews, Revisions, and Approvals

| Criteria added for new FDA indication: treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA) | 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 |
| 1Q 2020 annual review: criteria updated to include asthma pediatric expansion for age 6-11 years; added requirement that Nucala is not prescribed concurrently with other biologic therapies for asthma; references reviewed and updated. | 11.07.19 | 02.20 |
| 1Q 2021 annual review: criteria added for new FDA indication: hypereosinophilic syndrome indication (HES); updated Appendix B and D; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated. | 10.30.20 | 02.21 |

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.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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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.

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