Important Information

February 6, 2017

New Injectable Prior Authorization Approval - Mepolizumab (Nucala®)

Dear Provider,

Effective March 25, 2017, Mepolizumab (Nucala®) will be added to the non-Medicare list of injectable drugs requiring prior authorization. This letter is a notification of the upcoming requirement that providers must obtain prior authorization approval before administering this medication under the medical benefit.

Group Health requires prior authorization for a select group of injectable drugs that may be administered under the medical benefit in a physician’s office or by home infusion. These reviews are intended to ensure consistent benefit adjudication as well as appropriate utilization in accordance with the Group Health Pharmacy & Therapeutics Committee’s evidence-based criteria for coverage.

Prior Authorization Criteria for Mepolizumab (Nucala®):

See Appendix for inclusion and exclusion criteria details and criteria for continuation of therapy coverage.

Rationale:

- **Efficacy:** Efficacy of mepolizumab was established in three pivotal randomized, placebo-controlled studies in patients with severe asthma. These included a 52-week exacerbation and dose-ranging study (DREAM), a 32-week exacerbation study (MENSA), and an OCS reduction study (SIRIUS). Patients received mepolizumab or placebo as add-on drug therapy once every four weeks. The primary endpoint for DREAM and MENSA was the annualized rate of asthma exacerbations. Patients receiving mepolizumab had significantly fewer exacerbations versus placebo. In SIRIUS, the primary endpoint was reduction in OCS dose without loss of asthma control. Patients receiving mepolizumab had greater reductions in their daily maintenance OCS dose while maintaining asthma control versus placebo.

- **Safety:** The most common adverse effects with an incidence greater than or equal to 5% include headache, injection site reactions (pain, redness, swelling, itching, or a burning feeling at the injection site), back pain, and weakness (fatigue). The labeling warns that hypersensitivity reactions have occurred after the administration of mepolizumab and that herpes zoster infections have occurred in patients receiving the drug.

- **Value:** Although the studies demonstrated that mepolizumab can reduce the number of asthma exacerbations, there is uncertainty about whether the benefits will persist long-term.

Additional Information

A complete list of office-administered injectable drugs requiring prior authorization is available on MyGroupHealth for Contracted Providers at https://provider.ghc.org under Referrals & Clinical Review.

To request prior authorization review, please use the Referral Request online form on the provider website listed above. You can also fax your request to Review Services toll-free at 1-888-282-2685.
Thank you for the care you provide to our members, your patients. If you have any questions about this process, please call Review Services at 1-800-289-1363.

Sincerely,

Bruce Wilson, MD, Chair
Pharmacy & Therapeutics Committee

APPENDIX:

INCLUSION CRITERIA: Should fulfill ALL of the following to be eligible:

- Prescribing physician is an Allergist or Pulmonologist.
- Patient is at least 18 years of age.
- Clinical diagnosis of asthma indicated by airway reversibility, hyperresponsiveness or airway variability.
- Persistent airflow obstruction as indicated by:
  - Pre-bronchodilator forced expiratory volume in one second (FEV₁) <80% of the predicted value.
- Documentation of eosinophilic phenotype:
  - Blood eosinophil count of ≥500 cells/mcL in the past 30 days.
- Uncontrolled asthma (Table 1) despite an aggressive drug therapy regimen (Table 2) including:
  - High-dose inhaled corticosteroid (ICS), plus a long-acting beta-agonist (LABA), and requiring daily use of oral corticosteroid (OCS).
  OR
- Patients who are not using daily OCS but who otherwise meet the above criteria and who have had frequent (at least two) and/or severe exacerbations in the past 12 months requiring systemic corticosteroids for >3 days can be considered for mepolizumab.
Table 1: Indicators of Uncontrolled Asthma:

1. Two or more exacerbations in the past 12 months requiring systemic corticosteroids for >3 days.
2. Serious exacerbations: at least one hospitalization, ICU stay or mechanical ventilation in the past 12 months.
3. Asthma Control Test (ACT) is consistently <20

Table 2: Aggressive Drug Therapy Regimens:

<table>
<thead>
<tr>
<th>High-dose ICS</th>
<th>LABA</th>
<th>OCS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluticasone (Flovent HFA) 220 mcg: 2 puffs twice daily</td>
<td>Salmeterol (Serevent Diskus) 50 mcg: 1 inh twice daily</td>
<td>-</td>
</tr>
<tr>
<td>Mometasone DPI (Asmanex) 220 mcg: 2 inh twice daily</td>
<td>Formoterol (Foradil) 12 mcg: 1 inh twice daily</td>
<td>-</td>
</tr>
<tr>
<td>Mometasone (Asmanex HFA) 200 mcg: 2 puffs twice daily</td>
<td>-</td>
<td>Continuous OCS use</td>
</tr>
<tr>
<td>Combination ICS/LABA</td>
<td>-AND-</td>
<td>-</td>
</tr>
<tr>
<td>Mometasone 200 mcg/formoterol 5 mcg (<em>Dulera)</em>: 2 puffs twice daily</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Fluticasone 500 mcg/salmeterol 50 mcg (*Advair Diskus): 1 inh twice daily</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Fluticasone 230 mcg/salmeterol 21 mcg (*Advair HFA): 2 puffs twice daily</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Fluticasone 200 mcg/vilanterol 25 mcg (*Breo Ellipta): 1 inh once daily</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Budesonide 160 mcg/formoterol 4.5 mcg (*Symbicort): 2 puffs twice daily</td>
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</tbody>
</table>

DPI = dry powder inhaler; HFA = hydrofluoroalkane; ICS = inhaled corticosteroids; LABA = long acting beta-agonist; OCS = oral corticosteroids; inh = inhalations

*Dulera preferred

- Corticosteroid adverse effects: If a patient has been poorly controlled over at least one year and is experiencing corticosteroid side effects despite aggressive drug therapy (Table 2), then mepolizumab may be considered.

- Adherence: Patient should be at least 75% adherent to asthma drug therapies and with clinic follow-up appointments.
  - Drug therapy adherence should be at least 75% (calculated by day supply dispensed over the total number of days since treatment was started). If adherence is an issue, it should be addressed prior to considering mepolizumab.

- Evaluation of trigger avoidance measures and control of comorbid factors should be made prior to initiation of mepolizumab. Patient has uncontrolled asthma despite the following:
1. Eliminating all triggers from the home (e.g., pets, dust mites, foods, pollen, smoke, etc.)
2. Ruling out comorbid factors or other pulmonary disease (e.g., allergy, sinusitis, gastroesophageal reflux disease, anxiety disorder, panic disorder, vocal cord dysfunction, etc.)

**EXCLUSION CRITERIA:** If ONE or more of the criteria is met, patient is NOT eligible:

- History of hypersensitivity to mepolizumab or excipients in the formulation.
- Current smokers or former smokers with a smoking history of ≥10 pack-years.
- Presence of a known pre-existing, clinically important lung condition other than asthma (e.g., chronic obstructive pulmonary disease, bronchiectasis, pulmonary fibrosis, lung cancer).
- A current malignancy or previous history of cancer in remission for less than 12 months prior to starting therapy.
- Severe or clinically significant cardiovascular disease uncontrolled with standard treatment.
- Known, pre-existing, clinically significant endocrine, autoimmune, metabolic, neurological, renal, gastrointestinal, hepatic, hematological or any other system abnormalities that are uncontrolled with standard treatment.
- Patients with other conditions that could lead to elevated eosinophils such as hypereosinophilic syndromes, including Churg-Strauss Syndrome, eosinophilic esophagitis, allergic bronchopulmonary aspergillosis.
- Patients with known immunodeficiency (e.g., HIV) other than explained by being on corticosteroids taken for asthma.
- Patients with a known pre-existing parasitic infection
  - Treat patients with pre-existing helminth infections before initiating therapy with mepolizumab. If patient becomes infected while receiving treatment with mepolizumab and does not respond to anti-helminth treatment, discontinue treatment with mepolizumab until infection resolves.
- Patients who received omalizumab within the past 130 days or any monoclonal antibody to treat inflammatory disease within 5 half-lives.
- Patients with an allergy or intolerance to a monoclonal antibody or biologic.
- Patients who have known evidence of lack of adherence to controller medications and/or inability to follow physician’s recommendations.

**RELATIVE EXCLUSIONS:** The clinician may use their discretion for the following:

- History of alcohol/substance abuse within the past 2 years.
- Women who are pregnant or breastfeeding (refer to product labeling for further details):
  - The data on pregnancy exposure from the clinical trials are insufficient to inform on drug-associated risk. Mepolizumab is expected to cross the placenta; potential effects to the fetus may be greater in the second and third trimester of pregnancy. There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to mepolizumab.
Breastfeeding: It is not known if mepolizumab can be detected in breast milk; however, endogenous immune globulin is present in small amounts. According to the manufacturer, the developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for mepolizumab and any potential adverse effects on the breastfed infant from mepolizumab or from the underlying maternal condition.

- Serum IgE is less than or equal to 30 units/mL:
  - In a subgroup analysis patients with a baseline serum IgE concentration less than or equal to 30 units/mL did not have a reduction in exacerbation frequency compared with placebo.

**Evaluation for Continuation of Therapy**

- Evaluate response after 28 weeks (prior to the 7th dose) and then annually thereafter.
- Will not be re-approved if there is no improvement in any of the following:
  - Exacerbation frequency (defined as worsening of asthma that requires increase in ICS dose or treatment with systemic corticosteroids)
  - Objective improvement in quality of life: minimally important difference of 3 points on the Asthma Control Test or 0.5 points on the Asthma Control Questionnaire.
  - Sustained clinical improvement from reduced asthma symptoms (such as reduced missed days from work or school) or stable asthma control.