RECOMMENDATIONS
Based on the available clinical and economic evidence, Partners recommends that mepolizumab be eligible for formulary addition, with the following restrictions:

1. Indication for use
   • Add-on maintenance treatment of patients aged 18 years and older with severe, uncontrolled asthma with eosinophilic inflammation as defined below:
     
     - **Severe asthma:** Documented requirement for one of the following in the 6 months prior to therapy initiation
       - Regular treatment with oral corticosteroid (5 to 35 mg/day prednisone or equivalent)
       - High-dose inhaled corticosteroid (ICS) (at least 880 mcg/day FP ex-actuator or equivalent) plus LABA plus one other daily controller medication; patients should be adherent to these medications (80% of daily doses) for at least 6 months before adding mepolizumab and remain on these medications during mepolizumab treatment (See Medications below for additional information)

     - **Uncontrolled asthma** defined by at least two of the following in the past year:
       - Two or more exacerbations requiring bursts of OCS therapy for at least four days
       - At least one serious exacerbation requiring hospitalization or ED visit
       - Airflow limitation (FEV1 less than 80% predicted)
       - Poor symptom control (ACQ more than 1.5; ACT less than 20)

     - **Eosinophilic inflammation:**
       - Blood eosinophil level of at least 300 cells/microliters at initiation of therapy
       - Historical level of at least 300 cells/microliter in the last 15 months if it is documented that the patient is currently on oral steroids

   • Treatment should be initiated by allergy or asthma specialist with experience in the diagnosis and treatment of severe refractory eosinophilic asthma

   • Mepolizumab is NOT indicated for treatment of other eosinophilic conditions or for the relief of acute bronchospasm or status asthmaticus.

Medications:
   a. Patient must be maintained on and adherent to (taking at least 80% of daily doses) **high dose** inhaled steroids such as the following:

<table>
<thead>
<tr>
<th></th>
<th>Adults</th>
<th>Budesonide (Pulmicort®)</th>
<th>Flunisolide (AeroBID®)</th>
<th>Fluticasone (Flovent®)</th>
<th>Mometasone (Asmanex®)</th>
<th>Triamcinolone (Azmacort®)</th>
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<tbody>
<tr>
<td>Beclomethasone (QVAR®, Beclovent®, Vanceril®)</td>
<td>&gt;480 mcg/d</td>
<td>&gt;1200mcg/d</td>
<td>&gt;2000mcg/d</td>
<td>&gt;660mcg/d</td>
<td>&gt;400mcg/d</td>
<td>&gt;1500mcg/d</td>
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   - a long-acting bronchodilator (e.g., Serevent®, Foradil®, Arcapta® Neohaler®, etc.)
   - a leukotriene modifier (e.g., Singular®®, Accolate®, or Zyflo®)

   OR
• high dose Advair Diskus® (> 500/50; twice daily) or
  high dose Advair HFA® (≥ 115/21; 2 puffs twice daily) or
  high dose Symbicort® (≥ 160/4.5; 2 puffs twice daily) or
  high dose Dulera® (≥ 200/5; 2 puffs twice daily)
  OR
• daily systemic steroid therapy

b. Patient has at least 1 claim in the last 6 months for a bronchodilator to control acute symptoms (such as albuterol, Alupent®, Maxair®, Proventil®, Ventolin®, Xopenex®, etc.)

2. Cautions
  o **Opportunistic Infections**: Herpes zoster infections have occurred in patients receiving mepolizumab. Consider varicella vaccination if medically appropriate prior to starting therapy.

  o **Parasitic (Helminth) Infection**: Treat patients with pre-existing helminth infections before therapy with mepolizumab. If patients become infected while receiving treatment with mepolizumab and do not respond to anti-helminth treatment, discontinue mepolizumab until parasitic infection resolves.

3. Administration
  o Administration is restricted to outpatient use by trained staff able to manage hypersensitivity reactions or anaphylaxis.

4. Discontinuation
  o Treatment response should be globally assessed by the treating physician taking into consideration any improvement in asthma control, reduction in exacerbations and unscheduled healthcare utilization and improvement in quality of life of the patient.

  o If a patient does not respond within 4 doses of initiating treatment, it is unlikely that further administration of mepolizumab will be beneficial.
4. Discontinuation

- Treatment response should be globally assessed by the treating physician taking into consideration any improvement in asthma control, reduction in exacerbations and unscheduled healthcare utilization and improvement in quality of life of the patient.

- If a patient does not respond within 4 doses of initiating treatment, it is unlikely that further administration of mepolizumab will be beneficial.