Executive Summary

**Purpose:** Ensure appropriate utilization and control of Empaveli™ (pegcetacoplan)

**Why Issue Selected:** On May 14, 2021 the FDA approved Empaveli (pegcetacoplan) for the treatment of adult patients with paroxysmal nocturnal hemoglobinuria (PNH), an acquired life-long condition in which hematopoietic stem cells and their cellular progeny have lost the ability to anchor certain proteins to the cell surface. PNH has an incidence of 1 to 10 cases per million population, equating to 5,000-6,000 patients in the United States and mostly affects adults with a median age of onset in the 30s, although it has been reported in children. It may develop on its own (primary PNH) or in the context of other bone marrow disorders such as aplastic anemia (secondary PNH) and may be categorized as hemolytic PNH (classical), subclinical PNH, and PNH with bone marrow failure due to the lack of protective proteins CD55 and CD59 on the surface of red blood cells, PNH leads to chronic and/or paroxysmal intravascular hemolysis and propensity for thrombosis. Clinical manifestations include hemolytic anemia, fatigue, dyspnea, abdominal pain, chest pain, thrombosis, renal insufficiency, and pulmonary hypertension. The American Society of Hematology recommends using complement inhibitors when treating patients with symptomatic hemolytic PNH (including those with thrombosis, organ dysfunction, or pain) who do not have severe bone marrow failure. When compared with transplantation or supportive care alone, complement inhibitors offer a more favorable profile of toxicity and efficacy for hemolytic PNH.

Empaveli binds to complement protein C3 and its activation fragment C3b, thereby regulating the cleavage of C3 and the generation of downstream effectors of complement activation. Empaveli acts proximally in the complement cascade controlling both C3b-mediated extravascular hemolysis and terminal complement-mediated intravascular hemolysis.

Due to the high cost, possible adverse events, and specific approved indications, MO HealthNet will impose clinical criteria to ensure appropriate utilization of Empaveli.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Cost per vial (MAC)</th>
<th>Cost per year (MAC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EMPAVELI 1080 MG/20 ML VIAL</td>
<td>$4,386.20</td>
<td>$456,164.80</td>
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</table>
Type of Criteria:  ☒ Increased risk of ADE  ☐ Preferred Drug List
☒ Appropriate Indications  ☒ Clinical Edit

Data Sources:  ☐ Only Administrative Databases  ☒ Databases + Prescriber-Supplied

Setting & Population

- Drug class for review: Empaveli (pegcetacoplan)
- Age range: All appropriate MO HealthNet participants aged 18 years or older

Approval Criteria

Initial Therapy:
- Participant is aged ≥ 18 years AND
- Prescribed by or in consultation with a hemato­logist, on­cologist, or immunology specialist or other specialist in the treated disease state AND
- Documented diagnosis of PNH as confirmed by laboratory findings such as flow cytometry, lactate dehydrogenase level of 1.5 times the upper limit of normal, bone marrow aspirate and biopsy AND
- Participant is transfusion-dependent (Hb ≤ 7 g/dL or Hb ≤ 9 g/dL and experiencing symptoms of anemia) OR
- Documentation of symptomatic thromboembolic complications (e.g., abdominal pain, shortness of breath, chest pain, end-organ damage)

Continuation of Therapy:
- Initial approval is for 6 months, renewal of prior authorization for up to 1 year may be given following documentation of one of the following:
  - Improvement or less than expected decline in fatigue and quality of life
  - Decrease in transfusion burden
  - Increase in Hb levels from baseline
  - Normalization of LDH levels.

Denial Criteria

- Therapy will be denied if all approval criteria are not met

Required Documentation

<table>
<thead>
<tr>
<th>Laboratory Results:</th>
<th>☐</th>
<th>Progress Notes:</th>
<th>☒</th>
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<tbody>
<tr>
<td>MedWatch Form:</td>
<td>☐</td>
<td>Other:</td>
<td>☒</td>
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</tbody>
</table>

Disposition of Edit

Denial: Exception code “0682” (Clinical Edit)
Rule Type: CE

Default Approval Period

6 months
References

- Brodsky, Robert A., MD. Treatment and Prognosis of Paroxysmal Nocturnal Hemoglobinuria. UpToDate.