Empaveli (pegcetacoplan)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the Empaveli (pegcetacoplan) drug policy is to ensure appropriate selection of patients for therapy based on product labeling, clinical guidelines, and clinical studies. The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Empaveli (pegcetacoplan) is indicated for the treatment of adult patients with paroxysmal nocturnal hemoglobinuria (PNH).

POLICY

Required Documentation

Submission of the following information is necessary to initiate the prior authorization review:

- For initial requests: Flow cytometry used to show results of glycosylphosphatidylinositol-anchored proteins (GPI-Aps) deficiency
- For continuation requests: chart notes or medical documentation supporting positive clinical response.

Criteria for Initial Approval

A. Empaveli (pegcetacoplan) may be considered **medically necessary** for the treatment of paroxysmal nocturnal hemoglobinuria (PNH) when all of the following criteria are met:
   1. The diagnosis of PNH was confirmed by detecting a deficiency of glycosylphosphatidylinositol-anchored proteins (GPI-APs) as demonstrated by either of the following:
      a. At least 5% PNH cells
      b. At least 51% of GPI deficient poly-morphonuclear cells

2. Flow cytometry is used to demonstrate GPI-anchored proteins deficiency

Approval will be for up to **6 months**

Continuation of Therapy
Empaveli (pegcetacoplan) may be considered **medically necessary** for the continued treatment of paroxysmal nocturnal hemoglobinuria (PNH) in members when there is no evidence of unacceptable toxicity or disease progression while on the current regimen and demonstrate a positive response to therapy (e.g., improvement in hemoglobin levels, normalization of lactate dehydrogenase [LDH] levels).

Approval will be for **12 months**

Empaveli is considered **not medically necessary** for members who do not meet the criteria set forth above.

Dosage and Administration
Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Quantity Limits:

Trade Name	Generic Name	Quantity Limit
Empaveli™	Pegcetacoplan	9 vials per 28 days

CLINICAL RATIONALE

Background
Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, acquired, clonal, nonmalignant hematologic disease characterized by complement-mediated hemolysis (with or without hemoglobinuria), fatigue, increased susceptibility to thrombosis, and some degree of bone marrow dysfunction. PNH is characterized by the destruction of red blood cells through activation of the complement system (hemolysis). PNH can appear at any age but is most often diagnosed in the 30s and 40s and 400-500 new cases of PNH are diagnosed each year. The disorder affects between 5,000 and 6,000 people in the United States.

Empaveli is the first targeted C3 complement inhibitor and the first self-administered therapy approved for PNH. Empaveli is intended for use under the guidance of a healthcare professional. After proper training in subcutaneous infusion, a patient may self-administer, or the patient's caregiver may administer, if a healthcare provider determines that it is appropriate. Empaveli acts proximally in the complement cascade controlling C3b-mediated extravascular hemolysis and terminal complement-mediated intravascular hemolysis. It is administered by subcutaneous infusion twice weekly via a commercially available infusion pump with a reservoir and is the first agent to target extravascular hemolysis. Soliris and Ultomiris are C5 inhibitors approved for PNH and are given intravenously. These agents are effective in preventing intravascular hemolysis only.

Efficacy
The efficacy of Empaveli in patients with PNH was demonstrated in a randomized, multicenter, head-to-head study in 80 adults with PNH that compared Empaveli to Soliris (eculizumab). The study enrolled patients with PNH who had been treated with a stable dose of eculizumab for at least the previous 3 months and with Hb levels less than 10.5 g/dL. There was a 4-week run-in period during which all patients continued to receive their current dose of eculizumab with the addition of twice-weekly 1080 mg Empaveli. Patients were then randomized to receive Empaveli 1080 mg twice weekly (n=41) or eculizumab (n=39) for the

duration of the 16-week randomized controlled period. Empaveli was superior to eculizumab for the primary endpoint of change from baseline in hemoglobin level at Week 16. The adjusted mean change from baseline in hemoglobin level was 2.37 g/dL in the group treated with EMPAVELI versus -1.47 g/dL in the eculizumab group (Figure 1), demonstrating an adjusted mean increase of 3.84 g/dL with EMPAVELI compared to eculizumab at Week 16 (95% CI, 2.33-5.34). Non-inferiority was demonstrated in the secondary endpoints of transfusion avoidance and change from baseline in absolute reticulocyte count. Following completion of the randomized, controlled period, all patients entered a 32-week open-label period and received monotherapy with Empaveli. Empaveli demonstrated sustained improvements in hemoglobin and transfusion avoidance at Week 48.

Safety

The most common adverse reactions (≥10%) observed with Empaveli were injection-site reactions, infections, diarrhea, abdominal pain, respiratory tract infection, viral infection, and fatigue. The most common serious adverse reaction in patients treated with EMPAVELI was infections (5%). Empaveli is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). The Empaveli REMS program is intended to mitigate the occurrence and morbidity associated with encapsulated bacterial infections by requiring prescribers to vaccinate patients against encapsulated bacteria as recommended at least 2 weeks prior to administering the first dose of Empaveli unless the risks of delaying therapy outweigh the risks of developing a serious infection. Empaveli is contraindicated in patients who are not currently vaccinated against certain encapsulated bacteria unless the risks of delaying treatment outweigh the risks of developing a serious bacterial infection with an encapsulated organism and in patients with unresolved serious infection caused by encapsulated bacteria.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- J3490 – unclassified drugs
- J3590 – unclassified biologics
- C9399 – unclassified drugs or biologicals

REFERENCES

- Empaveli [package insert]. Waltham, MA: Apellis Pharmaceuticals, Inc.; June 2021
- Hillmen P, Szer J, Weitz I, et al. Pegcetacoplan versus Eculizumab in Paroxysmal Nocturnal Hemoglobinuria. N Engl J Med. 2021Mar 18;384(11):1028-1037. PMID: 33730455. Available at: https://www.nejm.org/doi/full/10.1056/NEJMoa2029073 Accessed on June 22, 2021
- Parker CJ, Omine M, Richards S, et al. Diagnosis and management of paroxysmal nocturnal hemoglobinuria. Blood. 2005;106(12):3699-3709.
- Peffault de Latour R, et al. Forty-Eight Week Efficacy and Safety of Pegcetacoplan in Adult Patients with Paroxysmal Nocturnal Hemoglobinuria and Suboptimal Response to Prior Eculizumab Treatment. Abstract S174. EHA 2021.
- Hill A, et al. The incidence and prevalence of paroxysmal nocturnal hemoglobinuria (PNH) and survival of patients in Yorkshire. Blood. 2006; 108 (11):985. Accessed on June 24, 2021.

POLICY HISTORY

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