Reference number(s)
4739-A

STANDARD MEDICARE PART B MANAGEMENT

EMPAVELI (pegcetacoplan)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Empaveli is indicated for the treatment of adult patients with paroxysmal nocturnal hemoglobinuria (PNH).

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. DOCUMENTATION

The following documentation must be available, upon request, for all submissions:
A. For initial requests: flow cytometry used to show results of glycosylphosphatidylinositol-anchored proteins (GPI-APs) deficiency.
B. For continuation requests: Chart notes or medical record documentation supporting benefit from therapy.

III. CRITERIA FOR INITIAL APPROVAL

Paroxysmal nocturnal hemoglobinuria
Authorization of 6 months may be granted for treatment of paroxysmal nocturnal hemoglobinuria (PNH) when all of the following criteria are met:
A. The diagnosis of PNH was confirmed by detecting a deficiency of glycosylphosphatidylinositol-anchored proteins (GPI-APs) as demonstrated by either of the following:
    1. At least 5% PNH cells
    2. At least 51% of GPI-AP deficient poly-morphonuclear cells
B. Flow cytometry is used to demonstrate GPI-APs deficiency

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

Paroxysmal nocturnal hemoglobinuria

Authorization for 12 months may be granted when all of the following criteria are met:
A. The member is currently receiving therapy with Empaveli
B. The member is receiving benefit from therapy (e.g., improvement in hemoglobin levels, normalization of lactate dehydrogenase [LDH] levels)

V. DOSAGE AND ADMINISTRATION

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

VI. SUMMARY OF EVIDENCE

The contents of this policy were created after examining the following resources:
1. The prescribing information for Empaveli.
2. The available compendium
    a. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    b. Micromedex DrugDex
    c. American Hospital Formulary Service- Drug Information (AHFS-DI)
    d. Lexi-Drugs
    e. Clinical Pharmacology
3. Management of paroxysmal nocturnal hemoglobinuria in the era of complement inhibitory therapy.
4. Guidelines for the Diagnosis and Monitoring of Paroxysmal Nocturnal Hemoglobinuria and Related Disorders by Flow Cytometry.

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Empaveli are covered.

VII. EXPLANATION OF RATIONALE

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for using percentage of PNH cells or percentage of GPI-AP deficiency poly-morphonuclear cells can be found in the guidelines for diagnosis of PNH (Borowitz et al and Preis et al). Flow cytometry is the gold standard for assessing the percentage of GPI-AP deficient poly-morphonuclear cells. Classic PNH is defined as greater than 50% of GPI-AP deficient PMNs. It is also possible to diagnose PNH by assessing the percentage of PNH cells. Most clinical trials for the complement inhibitors required at least 10% PNH cells, but the trials associated with Ultomiris only required 5% PNH cells. Therefore, the baseline requirement for all complement inhibitor programs will be at least 5%.

VIII. REFERENCES

1. Empaveli [package insert]. Waltham, MA: Apellis Pharmaceuticals, Inc.; May 2021.
2. Parker CJ. Management of paroxysmal nocturnal hemoglobinuria in the era of complement inhibitory therapy. *Hematology.* 2011; 21-29.
3. Borowitz MJ, Craig F, DiGiuseppe JA, et al. Guidelines for the Diagnosis and Monitoring of Paroxysmal Nocturnal Hemoglobinuria and Related Disorders by Flow Cytometry. *Cytometry B Clin Cytom*. 2010: 78: 211-230.

4. Preis M, Lowrey CH. Laboratory tests for paroxysmal nocturnal hemoglobinuria (PNH). Am J Hematol. 2014;89(3):339-341.
5. Parker CJ. Update on the diagnosis and management of paroxysmal nocturnal hemoglobinuria. Hematology Am Soc Hematol Educ Program. 2016;2016(1):208-216.