Blue Cross Blue Shield Blue Care Network of Michigan

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Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

Effective Date: 06/08/2023

Empaveli™ (pegcetacoplan)

HCPCS: J3490

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved indication
   b. FDA approved age
   c. Prescribed by or in consultation with a hematologist
   d. Flow cytometric confirmation of PNH type III red cells
   e. Had at least 1 transfusion in 12 months preceding Empaveli
      OR
   f. Documented history of major adverse thrombotic vascular events from thromboembolism
      OR
   g. Patient has high disease activity defined as a lactic dehydrogenase (LDH) level ≥ 1.5 times the upper limit of normal with one of the following symptoms:
      i. Weakness
      ii. Fatigue
      iii. Hemoglobinuria
      iv. Abdominal pain
      v. Dyspnea
      vi. Hemoglobin < 10 g/dL
      vii. A major vascular event
      viii. Dysphagia
      ix. Erectile dysfunction
   h. Must not be used in combination with Soliris®, Ultomiris®, or other medications to treat PNH
   i. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list and/or BCBSM/BCN's prior authorization and step therapy documents

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period: One year at a time

c. Renewal Criteria: Clinical documentation must be provided to confirm that current criteria are met and that the medication is providing clinical benefit

***Note: Coverage may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information

- Empaveli is a complement inhibitor indicated for the treatment of adult patients with paroxysmal nocturnal hemoglobinuria (PNH).

- Paroxysmal nocturnal hemoglobinuria is a rare acquired hematopoietic stem cell disorder in which red blood cells undergo cell lysis prematurely mediated by the alternative pathway of complement (APC). PNH arises due to a somatic mutation of a the PIGA gene whose protein product is a glycosyl transferase. Glycosyl transferase is part of the biosynthetic pathway that generates glycosyl phospastidylinositol (GPI) that serves as an anchor for membrane bound proteins on hematopoietic lineage cells. The mutation in PIGA results in a lack of glycosyl transferase activity and near-complete or complete absence of expression of all proteins that are GPI-anchored including the complement inhibitory proteins CD55 and CD59. The deficiency of CD55 and CD59 cause the complement-mediated intravascular hemolysis characteristic of PNH.

- Phenotypic mosaicism of the peripheral blood is a characteristic feature of PNH and is based on quantitative differences in complement sensitivity. Cell complement sensitivity is divided into 3 types. PNH type I cells are defined by having normal sensitivity to complement-mediated lysis. PNH type II cells are moderately complement sensitive or 2 - 4 times more sensitive than normal. Finally, PNH type III cells are markedly complement sensitive or 15 - 25 times more sensitive than normal. Complement sensitivity varies greatly from patient to patient depending on their unique phenotypic mosaicism. Erythrocyte phenotype is clinically relevant as patients with primarily type II cells have a relatively benign clinical course. In contrast, those who have more type III cells, which are completely deficient in CD55 and CD59, will have a more severe clinical course due to increased complement-mediated hemolysis. There is no guideline recommended cutoffs for when PNH can be diagnosed based on percentage of PNH type III cells.

- For patients with high disease activity, PNH complications increase significantly. High disease activity is defined as an elevated LDH greater than or equal to 1.5 times the upper limit of normal with constitutional symptoms of weakness, fatigue, hemoglobinuria, abdominal pain, dyspnea, hemoglobin less than 10 g/dL, dysphagia, and erectile dysfunction. Patients with an elevated LDH and at least one additional symptom should begin treatment with Empaveli.

- Thrombolytic complications are the leading cause of morbidity and mortality in PNH. Acute thrombotic events require anticoagulation with heparin. If there is no contraindication, anticoagulation should continue indefinitely for a patient with PNH who has experienced a thromboembolic complication. Empaveli should be initiated if a patient has experienced a thrombotic vascular event. For patients being treated with Empaveli and no history of thromboembolic complications, prophylactic anticoagulation may be unnecessary, although it is recommended that anticoagulation continue for those patients who experienced a thromboembolic event prior to initiating therapy with Empaveli.

- Empaveli has been shown to decrease the number of blood transfusions required by patients and stabilize hemoglobin levels. It has been studied in patients receiving as few as 1 blood transfusion in 12 months.

- Empaveli has not been studied and there is no data to support use in combination with other medications used to treat PNH, such as, Ultomiris. However, for patients switching from Soliris, Empaveli should be initiated while continuing Soliris at its current dose. After 4 weeks, Soliris should be discontinued before continuing on Empaveli monotherapy.

References:

1. Empaveli [prescribing information]. Waltham, MA: Apellis Pharmaceuticals, Inc.; February 2023.
2. National Organization for Rare Disorders. Paroxysmal nocturnal hemoglobinuria. 2019. Available at: https://rarediseases.org/rare-diseases/paroxysmal-nocturnal-hemoglobinuria/. Accessed on May 17, 2020.
3. Parker CJ. Update on the diagnosis and management of paroxysmal nocturnal hemoglobinuria. Hematology Am Soc Hematol Educ Program. 2016 Dec 2; 2016 (1): 208 - 16.
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5. Sahin F, Akay OM, Ayer M, et al. Pesg PNH diagnosis, follow-up and treatment guidelines. Am J Blood Res. 2016; 6 (2): 19 – 27.
6. Borowitz MJ, Craig FE, DiGiuseppe JA, et al. Guidelines for the diagnosis and monitoring of paroxysmal nocturnal hemoglobinuria and related disorders by flow cytometry. Cytometry Part B (Clinical Cytometry). 2010; 78B: 211 – 30.
7. Luzzatto L & Gianfaldoni G. Recent advances in biological and clinical aspects of paroxysmal nocturnal hemoglobinuria. International J Hematology. 2006; 84: 104 - 12.
8. Hill A, Kelly RJ, & Hillmen P. Thrombosis in paroxysmal nocturnal hemoglobinuria. Blood. 2013; 121 (25): 4985 - 96.
9. Hillmen P, Szer J, Weitz I, et al. Pegcetacoplan versus Eculizumab in Paroxysmal Nocturnal Hemoglobinuria. NEJM. 2021 Mar 18; 384 (11): 1028 - 37.

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<tr><th colspan="3">Policy History</th></tr>
<tr><th>#</th><th>Date</th><th>Change Description</th></tr>
<tr><td>1.5</td><td>Effective Date: 06/08/2023</td><td>Annual review of criteria was performed, no changes were made</td></tr>
<tr><td>1.4</td><td>Effective Date: 06/09/2022</td><td>Annual review of criteria was performed, no changes were made</td></tr>
<tr><td>1.3</td><td>Effective Date: 08/02/2021</td><td>UM medical management system update for BCBS
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table></td></tr>
<tr><td>1.2</td><td>Effective Date: 06/28/2021</td><td>UM medical management system update for BCN
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<tr><td>1.1</td><td>Effective Date: 06/14/2021</td><td>UM medical management system update for MAPPO and BCNA
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<tr><td>1.0</td><td>Effective Date: 06/10/2021</td><td>New Policy</td></tr>
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** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*