PRIOR AUTHORIZATION POLICY

POLICY: Complement Inhibitors – Empaveli Prior Authorization Policy
- Empaveli™ (pegcetacoplan subcutaneous injection – Apellis)

REVIEW DATE: 05/29/2024

OVERVIEW

Empaveli, a complement C3 inhibitor, is indicated for the treatment of **paroxysmal nocturnal hemoglobinuria** (PNH) in adults.[1] Empaveli is given subcutaneously, via an infusion pump or an on-body injector.

Empaveli has a Boxed Warning regarding serious infections caused by encapsulated bacteria. Empaveli is only available through a restricted access program, Empaveli Risk Evaluation and Mitigation Strategy (REMS).

Disease Overview

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, genetic disorder of hematopoietic stem cells.[2,3] The mutation in the X-linked gene phosphatidylinositol glycan class A (PIGA) results in a deficiency in the glycosylphosphatidylinositol (GPI) protein, which is responsible for anchoring other protein moieties to the surface of the erythrocytes. Loss of anchoring of these proteins causes cells to hemolyze and leads to complications such as hemolytic anemia, thrombosis, and peripheral blood cytopenias. PNH is a clinical diagnosis that should be confirmed with peripheral blood flow cytometry to detect the absence or severe deficiency of GPI-anchored proteins on at least two lineages.[2,4] Prior to the availability of complement inhibitors, only supportive measures in terms of managing the cytopenias and controlling thrombotic risk were available. Supportive measures include platelet transfusion, immunosuppressive therapy for patients with bone marrow failure, use of erythropoietin for anemias, and aggressive anticoagulation.

Dosing Recommendations When Switching to Empaveli from Soliris® (eculizumab intravenous infusion)

For patients switching from Soliris® (eculizumab intravenous [IV] infusion) to Empaveli, initiate Empaveli while continuing Soliris at the current dose.[1] After 4 weeks, discontinue Soliris and continue Empaveli monotherapy. For patients switching from Ultomiris® (ravulizumab-cwzy IV infusion or subcutaneous injection), initiate Empaveli no more than 4 weeks after the last dose of Ultomiris. There is no information regarding dosing recommendations for patients switching from Fabhalta® (iptacopan capsule) to Empaveli.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Empaveli. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Empaveli as well as the monitoring required for adverse events and long-term efficacy, approval requires Empaveli to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Empaveli is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Paroxysmal Nocturnal Hemoglobinuria.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, and iv):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Paroxysmal nocturnal hemoglobinuria diagnosis was confirmed by peripheral blood flow cytometry results showing the absence or deficiency of glycosylphosphatidylinositol-anchored proteins on at least two cell lineages; AND
     - **iii.** For a patient transitioning to Empaveli from Soliris (eculizumab intravenous infusion), the prescriber attests that Soliris will be discontinued 4 weeks after starting Empaveli; AND
     - **iv.** The medication is prescribed by or in consultation with a hematologist.
   - **B)** Patient is Currently Receiving Empaveli. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Patient is continuing to derive benefit from Empaveli according to the prescriber; AND
       Note: Examples of benefit include increase in or stabilization of hemoglobin levels, decreased transfusion requirements or transfusion independence, reductions in hemolysis, improvement in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue score.
     - **iii.** The medication is prescribed by or in consultation with a hematologist.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Empaveli is not recommended in the following situations:

1. **Concomitant Use with Soliris (eculizumab intravenous infusion) for > 4 weeks.** There is no evidence to support concomitant use of Empaveli with Soliris. However, to reduce the risk of hemolysis from abrupt treatment discontinuation in a patient switching from Soliris to Empaveli, the patient should be initiated on Empaveli while continuing Soliris. After 4 weeks, discontinue Soliris and continue Empaveli monotherapy.

2. **Concomitant Use with Fabhalta (iptacopan capsule), Ultomiris (ravulizumab-cwvz intravenous infusion or subcutaneous injection), or Voydeya (danicopan tablets).** There is no evidence to support concomitant use of Empaveli with Fabhalta, Ultomiris, or Voydeya.

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Empaveli™ subcutaneous infusion [prescribing information]. Waltham, MA: Apellis; February 2024.
2. Cançado RD, da Silva Araújo A, Sandes AF, et al. Consensus statement for diagnosis and treatment of paroxysmal nocturnal haemoglobinuria. *Hematol Transfus Cell Ther*. 2021;43:341-348.
3. Shah N, Bhatt H. Paroxysmal Nocturnal Hemoglobinuria. [Updated 2023 Jul 31]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK562292/. Accessed September 5, 2023.
4. Roth A, Maciejewski J, Nishinura JI, et al. Screening and diagnostic clinical algorithm for paroxysmal nocturnal hemoglobinuria: Expert consensus. *Eur J Haematol*. 2018;101(1):3-11.