Drug Coverage Policy

Effective Date.....5/01/2024
Coverage Policy Number.....IP0194
Policy Title..... Empaveli

Complement Inhibitors – Empaveli

- Empaveli™ (pegcetacoplan subcutaneous injection – Apellis)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making patient coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Cigna Healthcare Coverage Policy

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 Another Complement Inhibitor
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 before continuing on monotherapy with Empaveli. For patients switching from Ultomiris® (ravulizumab-cwzy IV infusion or subcutaneous [SC] 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.

Medical Necessity Criteria

Empaveli is considered medically necessary when the following criteria are met:

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 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 an 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 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.
     - **iii.** The medication is prescribed by or in consultation with a hematologist.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based

literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

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 Solrisi 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) or Ultomiris (ravulizumab intravenous infusion or subcutaneous injection).** There is no evidence to support concomitant use of Empaveli with Fabhalta or Ultomiris.

References

1. Empaveli™ subcutaneous infusion [prescribing information]. Waltham, MA: Apellis; February 2023.
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.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	**Paroxysmal Nocturnal Hemoglobinuria:** Removed criterion related to vaccination requirements. Initial approval duration was changed from 4 months to 6 months. Criterion regarding patient transitioning to Empaveli from Soliris or Ultomiris was revised to remove Ultomiris. **Conditions Not Covered:** Criterion regarding concomitant use with Soliris or Ultomiris for > 4 weeks was revised to remove Ultomiris. Criterion regarding concomitant use of Empaveli with Fabhalta or Ultomiris was added.	5/1/2024

The policy effective date is in force until updated or retired.