Clinical Policy: Pegcetacoplan (Empaveli)

Reference Number: ERX.SPA.427
Effective Date: 05.14.21
Last Review Date: 02.22
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Pegcetacoplan (Empaveli™) is a C3/C3b complement inhibitor.

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

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Empaveli is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Paroxysmal Nocturnal Hemoglobinuria (must meet all)**:**

1. Diagnosis of PNH;
2. Prescribed by or in consultation with a hematologist;
3. Age ≥ 18 years;
4. Flow cytometry shows detectable glycosylphosphatidylinositol (GPI)-deficient hematopoietic clones or ≥ 10% PNH cells;
5. Documentation of hemoglobin < 10.5 g/dL;
6. Empaveli is not prescribed concurrently with another FDA-approved product for PNH (e.g., Soliris®, Ultomiris®), unless the member is in a 4-week period of cross-titration between Soliris and Empaveli;
   **Provider must submit attestation of the presence or absence of concomitant Soliris therapy*
7. Dose does not exceed 2,160 mg per week or 1,080 mg every 3 days (total 10 doses per month) with documentation of a lactate dehydrogenase (LDH) level greater than 2 times the upper limit of normal (ULN).

Approval duration: 6 weeks *(if within cross-titration period with Soliris),* or 6 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Paroxysmal Nocturnal Hemoglobinuria (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in any of the following parameters (a – f):
   a. Improved measures of intravascular hemolysis (e.g., normalization of lactate dehydrogenase);
   b. Reduced need for red blood cell transfusions;
   c. Increased or stabilization of hemoglobin levels;

d. Less fatigue;
e. Improved health-related quality of life;
f. Fewer thrombotic events;

3. Empaveli is not prescribed concurrently with another FDA-approved product for PNH (e.g., Soliris, Ultomiris);
4. If request is for a dose increase, new dose does not exceed 2,160 mg per week or 1,080 mg every 3 days (total 10 doses per month) with documentation of an LDH level greater than 2 times the ULN.

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
GPI: glycosylphosphatidylinositol
LDH: lactate dehydrogenase
PNH: paroxysmal nocturnal hemoglobinuria
REMS: Risk Evaluation and Mitigation Strategy
ULN: upper limit of normal

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): hypersensitivity to pegcetacoplan or any of the excipients; patients who are not currently vaccinated against certain encapsulated bacteria unless the risks of delaying Empaveli treatment outweigh the risks of developing a serious bacterial infection with an encapsulated organism; patients with unresolved serious infection caused by encapsulated bacteria
- Boxed warning(s): serious infections caused by encapsulated bacteria; Empaveli is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS)

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
PNH	1,080 mg by SC infusion twice weekly via a commercially available pump For patients switching from Soliris, initiate Empaveli while continuing Soliris at its current dose. After 4 weeks, discontinue Soliris before continuing on monotherapy with Empaveli. For patients switching from Ultomiris, initiate Empaveli no more than 4 weeks after the last dose of Ultomiris. For LDH levels > 2x ULN, adjust the dosing regimen to 1,080 mg every three days.	1,080 mg/dose

VI. Product Availability

Single-dose vial injection: 1,080 mg/20 mL

VII. References

1. Empaveli Prescribing Information. Waltham, MA: Apellis Pharmaceuticals, Inc.; May 2021. Available at: https://pi.apellis.com/files/PI_Empaveli.pdf. Accessed November 9, 2021.
2. Wong R, Pullon H, Deschatelets P, et al. Inhibition of C3 with APL-2 results in normalization of markers of intravascular and extravascular hemolysis in subjects with paroxysmal nocturnal hemoglobinuria (PNH). Poster presented at: American Society of Hematology (ASH). 2018. Available at: https://apellis.com/presentations/2018%20-%20ASH%20poster%20PNH.pdf.
3. Hillmen P, Szer J, Weitz IC, et al. Pegcetacoplan versus eculizumab in paroxysmal nocturnal hemoglobinuria. NEJM March 2021;384:1028-37.
4. Bhak RY, Mody-Patel N, Baver SB, et al. Comparative effectiveness of pegcetacoplan versus ravulizumab in patients with paroxysmal nocturnal hemoglobinuria previously treated with eculizumab: a matching-adjusted indirect comparison. Abstract 2581. Presented at the 62nd American Society of Hematology Annual Meeting and Exposition, Dec 2-11, 2020.
5. Parker C, Omine M, Richards S, et al. Diagnosis and management of paroxysmal nocturnal hemoglobinuria. Blood 2005; 106(12):3699-3709. doi:10.1182/blood-2005-04-1717.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	01.05.21	02.21
Drug is now FDA-approved – criteria updated per FDA labeling: modified restriction against concomitant use of Empaveli with Soliris by making an exception for the initial 4-week cross-titration phase; references reviewed and updated.	05.18.21	08.21
1Q 2022 annual review: increased the maximum recommended dose to accommodate patients who experience increased LDH levels, per dosing recommendations in the Empaveli PI; removed the requirement for initial approval for at least one RBC transfusion in the last 12 months since 25% of the patients in the PEGASUS trial had zero past transfusions and data from the trial did not show a difference in Empaveli effect for those patients; references reviewed and updated.	11.16.21	02.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.