Clinical Policy: Pegcetacoplan (Empaveli)

Reference Number: PA.CP.PHAR.524
Effective Date: 10/2021
Last Review Date: 07/2023

Coding Implications
Revision Log

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.

It is the policy of PA Health & Wellness® 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. Request is for Empaveli;
4. Age ≥ 18 years;
5. Flow cytometry shows detectable glycosylphosphatidylinositol (GPI)-deficient hematopoietic clones or ≥ 10% PNH cells;
6. Documentation of hemoglobin < 10.5 g/dL;
7. Empaveli is not prescribed concurrently with either of the following (a and b):
   a. Syfovre;
   b. 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*
   **Provider must submit attestation of the presence or absence of concomitant Soliris therapy*
8. 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 the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Request is for Empaveli;
3. 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;
4. Empaveli is not prescribed concurrently with either of the following (a and b):
   a. Syfovre;
   b. Another FDA-approved product for PNH (e.g., Soliris, Ultomiris);
5. 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 PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

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 policies – PA.CP.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AMD: age-related macular degeneration
DA: disk area
ETDRS: Early Treatment Diabetic Retinopathy Study
FDA: Food and Drug Administration
GA: geographic atrophy
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):
  - Empaveli: 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):
  - Empaveli: 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

Drug Name	Indication	Dosing Regimen	Maximum Dose
Empaveli	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.; Fabruary 2023. Available at: https://pi.apellis.com/files/PI_Empaveli.pdf. Accessed May 8, 2023.
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..
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.
6. Apellis Pharmaceuticals, Inc. Study of pegcetacoplan (APL-2) therapy in patients with geographic atrophy (FILLY). ClinicalTrials.gov. Available at: https://clinicaltrials.gov/ct2/show/NCT02503332. Accessed May 8, 2023.
7. Liao DS, Grossi FV, El Mehdi D, et al. Complement C3 inhibitor pegcetacoplan for geographic atrophy secondary to age-related macular degeneration: A randomized phase 2 trial. Ophthalmology. 2020; 127(2): 186-195.
8. Apellis Pharmaceuticals, Inc. Study to compare the efficacy and safety of intravitreal APL-2 therapy with sham injections in patients with geographic atrophy (GA) secondary to age-related macular degeneration (DERBY). ClinicalTrials.gov. Available at: https://clinicaltrials.gov/ct2/show/NCT03525600. Accessed May 8, 2023.
9. Apellis Pharmaceuticals, Inc. A study to compare the efficacy and safety of intravitreal APL-2 therapy with sham injections in patients with geographic atrophy (GA) secondary to age-related macular degeneration (OAKS). ClinicalTrials.gov. Available at: https://clinicaltrials.gov/ct2/show/NCT03525613. Accessed May 8, 2023.
10. Goldberg R, Heier JS, Wyoff CC, et al. Abstract: Efficacy of intravitreal pegcetacoplan in patients with geographic atrophy (GA): 12-month results from the phase 3 OAKS and DERBY studies. Investigative Ophthalmology & Visual Science. 2022; 63(7): 1500.
11. Apellis Pharmaceuticals, Inc. Apellis announces pegcetacoplan showed continuous and clinically meaningful effects at month 18 in phase 3 DERBY and OAKS studies for geographic atrophy (GA). News release published March 16, 2022. Available at: https://investors.apellis.com/news-releases/news-release-details/apellis-announces-pegcetacoplan-showed-continuous-and-clinically. Accessed May 8, 2023.
12. American Academy of Ophthalmology Retina/Vitreous Committee. Preferred Practice Pattern® Guidelines. Age-Related Macular Degeneration. San Francisco, CA: American Academy of Ophthalmology; 2019. Available at: https://www.aao.org/preferred-practice-pattern/age-related-macular-degeneration-ppp. Accessed May 8, 2023.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
C9399	Unclassified drugs or biologicals
J7799	Noc drugs, other than inhalation drugs, administered through DME

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	10/2021	
Added Empaveli is not prescribed concurrently with APL-2	10/2022	
1Q 2023 annual review: no significant changes; references reviewed and updated.	01/2023	
3Q 2023 annual review: no significant changes; references reviewed and updated.	07/2023	