

Clinical Policy: Pegcetacoplan (Empaveli)

Reference Number: PA.CP.PHAR.524

Effective Date: 10/2021

Last Review Date: 07/2026

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 $\geq$ 18 years;
5. Flow cytometry shows detectable glycosylphosphatidylinositol (GPI)-deficient hematopoietic clones or $\geq$ 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[®], Fabhalta[®], Voydeya[™], Bkemv[™], Epysqli[®], PiaSky[®]), unless the member is in a 4-week period of cross-titration between Soliris/Bkemv/Epysqli and Empaveli;*
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).

**Provider must submit attestation of the presence or absence of concomitant*

Soliris/Bkemv/Epysqli therapy

Approval duration:

If within cross-titration period with Soliris: 6 weeks

All other requests: 12 months

B. C3 Glomerulopathy, Primary Immune-Complex Membranoproliferative Glomerulonephritis (must meet all):

1. Diagnosis of one of the following confirmed via kidney biopsy (a or b):
 - a. C3G;

- b. Primary IC-MPGN, and member does not have recurrent disease following kidney transplant;
2. Request is for Empaveli;
3. Prescribed by or in consultation with a nephrologist;
4. Age ≥ 12 years;
5. Documentation of both of the following (a and b):
 - a. Urine protein-to-creatinine ratio (UPCR) ≥ 1 g/g;
 - b. Estimated glomerular filtration rate (eGFR) ≥ 30 mL/min/1.73 m²;
6. Failure of at least a 12-week trial of a renin-angiotensin-aldosterone system (RAAS) inhibitor (e.g., irbesartan, losartan, lisinopril, benazepril) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced (*see Appendix D*);
7. Empaveli is not prescribed concurrently with either of the following (a and b):
 - a. Syfovre;
 - b. Another FDA-approved product for C3G or IC-MPGN (e.g., Fabhalta);
8. Dose does not exceed one of the following (a, b, or c):
 - a. Adults and pediatric members weighing ≥ 50 kg: 1,080 mg twice per week;
 - b. Pediatric members weighing 35 kg to < 50 kg: 810 mg twice per week;
 - c. Pediatric members weighing < 35 kg: 648 mg twice per week.

Approval duration: 12 months

C. 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.PHARM.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 or extravascular hemolysis (e.g., normalization of lactate dehydrogenase, reduced absolute reticulocyte count, reduced bilirubin);
 - 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, Fabhalta, Voydeya, Bkembv, Epysqli, PiaSky);

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: 12 months

B. C3 Glomerulopathy, Primary Immune-Complex Membranoproliferative Glomerulonephritis (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.PHARM.01) applies;
2. Request is for Empaveli;
3. Member is responding positively to therapy as evidenced by one of the following (a or b):
 - a. Decrease in UPCR from baseline;
 - b. Reduction of proteinuria as evidence by a lower total urine protein per day from baseline;
4. Empaveli is not prescribed concurrently with either of the following (a and b):
 - a. Syfovre;
 - b. Another FDA-approved product for C3G or IC-MPGN (e.g., Fabhalta);
5. If request is for a dose increase, new dose does not exceed one of the following (a, b, or c):
 - a. Adults and pediatric members weighing ≥ 50 kg: 1,080 mg twice per week;
 - b. Pediatric members weighing 35 kg to < 50 kg: 810 mg twice per week;
 - c. Pediatric members weighing < 35 kg: 648 mg twice per week.

Approval duration: 12 months

C. 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.PHARM.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

C3G: C3 glomerulopathy

DA: disk area

ETDRS: Early Treatment Diabetic

Retinopathy Study

FDA: Food and Drug Administration

GA: geographic atrophy

GPI: glycosylphosphatidylinositol

IC-MPGN: immune-complex
membranoproliferative
glomerulonephritis
LDH: lactate dehydrogenase
PNH: paroxysmal nocturnal hemoglobinuria

RAAS: renin-angiotensin-aldosterone
system
REMS: Risk Evaluation and Mitigation
Strategy
ULN: upper limit of normal

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Maximum Dose
Angiotensin-converting enzyme inhibitors (ACEIs)		
benazepril (Lotensin [®])	Various	80 mg/day
captopril (Capoten [®])	Various	450 mg/day
enalapril (Vasotec [®] , Epaned [®])	Various	40 mg/day
fosinopril (Monopril [®])	Various	80 mg/day
lisinopril (Prinivil [®] , Zestril [®] , Qbrelis [®])	Various	80 mg/day
moexipril (Univasc [®])	Various	30 mg/day
perindopril (Aceon [®])	Various	16 mg/day
quinapril (Accupril [®])	Various	80 mg/day
ramipril (Altace [®])	Various	20 mg/day
trandolapril (Mavik [®])	Various	8 mg/day
Angiotensin receptor blockers (ARBs)		
azilsartan (Edarbi [®])	Various	80 mg/day
candesartan (Atacand [®])	Various	32 mg/day
eprosartan (Teveten [®])	Various	900 mg/day
irbesartan (Avapro [®])	Various	300 mg/day
losartan (Cozaar [®])	Various	100 mg/day
olmesartan (Benicar [®])	Various	40 mg/day
telmisartan (Micardis [®])	Various	80 mg/day
valsartan (Diovan [®])	Various	320 mg/day

Therapeutic alternatives are listed as Brand name[®] (generic) when the drug is available by brand name only and generic (Brand name[®]) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
 - Empaveli: hypersensitivity to pegcetacoplan or any of the excipients; for initiation in patients with unresolved serious infection caused by encapsulated bacteria including *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type B
- 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)

Appendix D: General Information

- The 2021 Kidney Disease Improving Global Outcomes (KDIGO) glomerular disease guideline recommends supportive therapy with a RAAS inhibitor (ACEI or ARB) as first line for all patients with glomerulonephritis (such as C3G and IC-MPGN) and proteinuria.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
PNH	1,080 mg by SC twice weekly via a commercially available pump infusion pump or the Empaveli on body injector For patients switching from Soliris/Bkemv/Epysqli, initiate Empaveli while continuing Soliris/Bkemv/Epysqli at its current dose. After 4 weeks, discontinue Soliris/Bkemv/Epysqli 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
C3G, primary IC-MPGN	Adults and pediatric members weighing ≥ 50 kg: 1,080 mg SC twice weekly Pediatric members weighing 35 kg to < 50 kg: 810 mg SC twice weekly Pediatric members weighing < 35 kg: 648 mg SC twice weekly	See regimen

VI. Product Availability

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

VII. References

1. Empaveli Prescribing Information. Waltham, MA: Apellis Pharmaceuticals, Inc.; February 2024. Available at: <https://empavelihcp.com/>. Accessed April 17, 2026.
PNH
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.
C3G/Primary IC-MPGN
 6. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. KDIGO 2021 clinical practice guideline for the management of glomerular diseases. *Kidney Int.* 2021 Oct;100(4S):S1-S276. doi: 10.1016/j.kint.2021.05.021.
 7. Vivarelli M, Barratt J, Beck LH, et al. The role of complement in kidney disease: Conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. *Kidney International.* 2024; 106: 369-391.

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
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
3Q 2024 annual review: for PNH, added Fabhulta, Voydeya, and Bkenv to the list of therapies that Empaveli should not be prescribed concurrently with; revised Empaveli contraindications in Appendix C per updated prescribing information; references reviewed and updated.	07/2024
3Q 2025 annual review: for PNH, added Epysqli and PiaSky to the list of therapies that Empaveli should not be prescribed concurrently with, added improvement of extravascular hemolysis as an example of positive response to therapy, and revised continued approval duration from 6 to 12 months as PNH is a chronic condition; references reviewed and updated.	07/2025

Reviews, Revisions, and Approvals	Date
3Q 2026 annual review: RT4: added criteria for new FDA-approved indication of C3G/primary IC-MPGN for Empaveli; for PNH and C3G/primary IC-MPGN, revised all approval durations to 6 to 12 months; references reviewed and updated.	07/2026