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Section:	Prescription Drugs	**Effective Date:**	April 1, 2026
Subsection:	Hematological Agents	**Original Policy Date:**	June 4, 2021
Subject:	Empaveli	**Page:**	1 of 6

Last Review Date: March 6, 2026

Empaveli

Description

Empaveli (pegcetacoplan)

Background
Empaveli (pegcetacoplan) is a complement inhibitor indicated for the treatment of paroxysmal nocturnal hemoglobinuria (PNH) and C3 glomerulopathy (C3G) or primary immune-complex membranoproliferative glomerulonephritis (IC-MPGN). Empaveli binds to complement protein C3 and its activation fragment C3b, thereby regulating the cleavage of C3 and the generation of downstream effectors of complement activation. In paroxysmal nocturnal hemoglobinuria (PNH), extravascular hemolysis (EVH) is facilitated by C3b opsonization while intravascular hemolysis (IVH) is mediated by downstream membrane attack complex. Empaveli acts proximally in the complement cascade controlling both C3b-mediated EVH and terminal complement-mediated IVH. In C3G and primary IC-MPGN, complement dysregulation and overactivation causes deposition of C3 fragments in glomeruli, which contributes to the pathogenesis of C3G and is thought to contribute to the pathogenesis of IC-MPGN. Empaveli binds C3 and its activation fragment C3b, therefore inhibiting C3 activation, decreasing C3 glomerular fragment deposition, and decreasing C5 convertase activity and subsequent assembly of C5b-9 (1).

Regulatory Status
FDA-approved indication: Empaveli is a complement inhibitor indicated: (1)

- for the treatment of adult patients with paroxysmal nocturnal hemoglobinuria (PNH).

- for the treatment of adult and pediatric patients aged 12 years and older with C3 glomerulopathy (C3G) or primary immune-complex membranoproliferative glomerulonephritis (IC-MPGN), to reduce proteinuria.

Empaveli has a boxed warning regarding serious infections caused by encapsulated bacteria. Infections caused by encapsulated bacteria, such as *Streptococus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type B may occur in patients treated with Empaveli and may become rapidly life-threatening or fatal if not recognized and treated early. Patients should be vaccinated against encapsulated bacteria at least 2 weeks prior to initiation of Empaveli therapy according to current Advisory Committee on Immunization Practices (ACIP) guidelines. Because of the risk of serious infections caused by encapsulated bacteria, Empaveli is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Empaveli REMS. Under the Empaveli REMS, prescribers must enroll in the program (1).

Empaveli also has warnings regarding infusion-related reactions, monitoring PNH manifestations after discontinuation of Empaveli, and interference of laboratory tests (1).

Empaveli may cause embryo-fetal harm when administered to a pregnant woman. Pregnancy testing is recommended for females of reproductive potential prior to treatment with Empaveli. Female patients of reproductive potential should be advised to use effective contraception during treatment with Empaveli and for 40 days after the last dose (1).

The safety and effectiveness of Empaveli in pediatric patients less than 18 years of age with PNH have not been established. The safety and effectiveness of Empaveli in pediatric patients less than 12 years of age with C3G or IC-MPGN have not been established (1).

Related policies
Fabhalta, Soliris, Ultomiris

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Empaveli may be considered **medically necessary** if the conditions indicated below are met.

Empaveli may be considered **investigational** for all other indications.

Prior-Approval Requirements

Diagnoses

Patient must have **ONE** of the following:

1. Paroxysmal nocturnal hemoglobinuria (PNH)
   a. 18 years of age or older
   b. Documented baseline value for hemoglobin (Hgb)
   c. **NO** dual therapy with another Prior Authorization (PA) medication for PNH (see Appendix 1)

2. Complement 3 glomerulopathy (C3G) or primary immune-complex membranoproliferative glomerulonephritis (IC-MPGN)
   a. 12 years of age or older
   b. Diagnosis has been confirmed by a kidney biopsy
   c. Used to reduce proteinuria
   d. Documented baseline urine protein-to creatinine ration (UPCR)
   e. Used in combination with maximum recommended or maximum tolerated dose of ACEI or ARB therapy

AND ALL of the following:

a. Vaccination against encapsulated bacteria, including *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type B at least 2 weeks prior to initiation [unless Empaveli (pegcetacoplan) treatment cannot be delayed]
b. Prescriber is enrolled in Empaveli REMS program

Prior – Approval *Renewal* Requirements

Diagnoses

Patient must have **ONE** of the following:

1. Paroxysmal nocturnal hemoglobinuria (PNH)
   a. 18 years of age or older
   b. Increase in hemoglobin (Hgb) from pretreatment baseline
   c. **NO** dual therapy with another Prior Authorization (PA) medication for PNH (see Appendix 1)

2. Complement 3 glomerulopathy (C3G) or primary immune-complex membranoproliferative glomerulonephritis (IC-MPGN)
   a. 12 years of age or older
   b. Decrease in urine protein-to-creatinine ratio (UPCR)
   c. Used in combination with maximum recommended or maximum tolerated dose of ACEI or ARB therapy

AND ALL of the following:
   a. Prescriber is enrolled in Empaveli REMS program
   b. Absence of unacceptable toxicity from the drug

Policy Guidelines

Pre – PA Allowance

None

Prior - Approval Limits

Quantity 30 vials every 90 days

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Empaveli (pegcetacoplan) is a complement inhibitor indicated for the treatment of paroxysmal nocturnal hemoglobinuria (PNH) and C3 glomerulopathy (C3G) or primary immune-complex membranoproliferative glomerulonephritis (IC-MPGN). Empaveli has a boxed warning citing the risk of serious infections caused by encapsulated bacteria and it is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). Empaveli also has warnings regarding infusion-related reactions, monitoring PNH manifestations after discontinuation of Empaveli, and interference of laboratory tests. The safety and effectiveness of Empaveli in pediatric patients less than 18 years of age with PNH have not been established. The safety and effectiveness of Empaveli in pediatric patients less than 12 years of age with C3G or IC-MPGN have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Empaveli while maintaining optimal therapeutic outcomes.

References

1. Empaveli [package insert]. Waltham, MA: Apellis Pharmaceuticals, Inc.; July 2025.

Policy History

Date	Action
June 2021	Addition to PA
September 2021	Annual review
March 2022	Annual review
March 2023	Annual review and reference update. Changed policy number to 5.85.042
June 2023	Annual review
December 2023	Annual review and reference update
March 2024	Annual review
June 2024	Annual editorial review and reference update
September 2024	Annual review
December 2024	Annual review
March 2025	Annual review
June 2025	Annual review
September 2025	Annual review. Per PI update, added indication of CG3 or IC-MPGN
March 2026	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 6, 2026 and is effective on April 1, 2026.

Appendix 1 - List of PA Medications for PNH

Generic Name	Brand Name
eculizumab	Soliris
iptacopan	Fabhalta
pegcetacoplan	Empaveli
ravulizumab-cwvz	Ultomiris