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5.85.042

Section:	Prescription Drugs	**Effective Date:**	April 1, 2024
Subsection:	Hematological Agents	**Original Policy Date:**	June 4, 2021
Subject:	Empaveli	**Page:**	1 of 5

Last Review Date: March 8, 2024

Empaveli

Description

Empaveli (pegcetacoplan)

Background
Empaveli (pegcetacoplan) is a complement inhibitor indicated for the treatment of paroxysmal nocturnal hemoglobinuria (PNH). 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 (1).

Regulatory Status
FDA-approved indication: Empaveli is a complement inhibitor indicated for the treatment of adult patients with paroxysmal nocturnal hemoglobinuria (PNH) (1).

Empaveli has a boxed warning regarding serious infections caused by encapsulated bacteria. Meningococcal infections may occur in patients treated with Empaveli and may become rapidly life-threatening or fatal if not recognized and treated early. Use of Empaveli may predispose individuals to serious infections, especially those caused by encapsulated bacteria, such as *Streptococcus pneumoniae*, *Neisseria meningitidis* types A, C, W, Y, and B, and *Haemophilus influenzae* type B. Patients should be vaccinated against encapsulated bacteria, including *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type B at least

2 weeks prior to initiation of Empaveli therapy according to current Advisory Committee on Immunization Practices (ACIP) guidelines. Vaccination reduces, but does not eliminate, the risk of serious infections (1).

Empaveli is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (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 have not been established (1).

Related policies
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

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Paroxysmal nocturnal hemoglobinuria (PNH)

AND ALL of the following:

a. Documented baseline value for hemoglobin (Hgb)
b. 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]
c. Prescriber is enrolled in Empaveli REMS program
d. **NO** dual therapy with another terminal complement inhibitor (see Appendix 1)

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Paroxysmal nocturnal hemoglobinuria (PNH)

AND ALL of the following:

a. Increase in hemoglobin (Hgb) from pretreatment baseline
b. Prescriber is enrolled in Empaveli REMS program
c. Absence of unacceptable toxicity from the drug
d. **NO** dual therapy with another terminal complement inhibitor (see Appendix 1)

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). 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 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.; September 2023.

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

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 8, 2024 and is effective on April 1, 2024.

Appendix 1 - List of Terminal Complement Inhibitors

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