Evolent Clinical Guideline 3098 for Empaveli™ (pegcetacoplan)

Guideline Number: Evolent_CG_3098	**Applicable Codes**	
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STATEMENT

Purpose

To define and describe the accepted indications for Empaveli (pegcetacoplan) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

INDICATIONS

Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided

- The member has not experienced disease progression on the requested medication AND
- The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization AND
- Additional medication(s) are not being added to the continuation request.

Paroxysmal Nocturnal Hemoglobinuria (PNH)

- The member has a confirmed diagnosis of Paroxysmal Nocturnal Hemoglobinuria (PNH) and Empaveli (pegcetacoplan) is being used to treat the member's hemolytic anemia due to PNH.

CONTRAINDICATIONS/WARNINGS

- Contraindications
  - Hypersensitivity to pegcetacoplan or any component of the formulation
  - Initiation in patients with unresolved serious infection caused by encapsulated bacteria including *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type B
- US Boxed Warning
  - Pegcetacoplan, a complement inhibitor, increases the risk of serious infections, especially those caused by encapsulated bacteria, such as *Streptococcus*

pneumoniae, *Neisseria meningitidis*, and *Haemophilus influenzae* type B. Life-threatening and fatal infections with encapsulated bacteria have occurred in patients treated with complement inhibitors. These infections may become rapidly life-threatening or fatal if not recognized and treated early.

- Complete or update vaccination for encapsulated bacteria at least 2 weeks prior to the first dose of pegcetacoplan unless the risks of delaying therapy with pegcetacoplan outweigh the risk of developing a serious infection. Comply with the most current Advisory Committee on Immunization Practices recommendations for vaccinations against encapsulated bacteria in patients receiving a complement inhibitor.
- Patients receiving pegcetacoplan are at increased risk for invasive disease caused by encapsulated bacteria, even if they develop antibodies following vaccination. Monitor patients for early signs and symptoms of serious infections and evaluate immediately if infection is suspected.

- Because of the risk of serious infections caused by encapsulated bacteria, pegcetacoplan is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the EMPAVELI REMS.

EXCLUSION CRITERIA

- Lack of improvement in Hgb of 2.0 gm/dl or more at 16 weeks while taking Empaveli (pegcetacoplan).
- Concurrent administration with Soliris (eculizumab) beyond 4 weeks of Empaveli (pegcetacoplan) treatment. When switching from Soliris (eculizumab) to Empaveli (pegcetacoplan), a 4- week run in period is recommended to reduce the risk of hemolysis with abrupt discontinuation.
- Dosing exceeds single dose limit of Empaveli (pegcetacoplan) 1,080 mg.
- Investigational use of Empaveli (pegcetacoplan) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:
  - Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
  - Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
  - Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
  - Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in

some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).

- That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
- That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
- That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

CODING AND STANDARDS

Codes

- J2781 - Injection, pegcetacoplan, intravitreal, 1 mg

Applicable Lines of Business

☐	CHIP (Children's Health Insurance Program)
☒	Commercial
☒	Exchange/Marketplace
☒	Medicaid
☐	Medicare Advantage

POLICY HISTORY

Date	Summary
May 2026	• Updated references
May 2025	• Converted to new Evolent guideline template • This guideline replaces UM ONC_1439 Empaveli (pegcetacoplan) • Updated references
May 2024	• Updated NCH verbiage to Evolent

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Specialty Services Clinical Guideline Review Committee

Disclaimer

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. Evolent clinical guidelines contain guidance that requires prior authorization and service limitations. A list of procedure codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.

REFERENCES

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9. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: **https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf**.
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