Original Effective Date: 07/15/2021
Current Effective Date: 08/30/2023
Last P&T Approval/Version: 07/26/2023
Next Review Due By: 07/2024
Policy Number: C21423-A

Empaveli (pegcetacoplan)

PRODUCTS AFFECTED

Empaveli (pegcetacoplan)
*Syfovre (pegcetacoplan) – SEE SYFOVRE (PEGCETACOPLAN INTRAVITREAL) MHI C25311-A

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Paroxysmal nocturnal hemoglobinuria (PNH)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review.

A. PAROXYSMAL NOCTURNAL HEMOGLOBINURIA (PNH):
1. Documented diagnosis of Paroxysmal nocturnal hemoglobinuria (PNH)
   AND
2. Prescriber attests that member has been vaccinated against *Streptococcus pneumoniae*,

Neisseria meningitidis, and *Haemophilus influenzae* type B (at least 2 weeks prior to pegcetacoplan treatment, if not previously vaccinated).
AND

3. Documentation of baseline labs and status [DOCUMENTATION REQUIRED]:
   a. Hemoglobin level
      AND
   b. Documentation of Lactate dehydrogenase (LDH) level which is 1.5 times the upper limit of the normal range (within the last 30 days). Submit laboratory results with reference range.
      AND
   c. Documentation that member is transfusion-dependent, defined by having a transfusion within the last 12 months and ONE of the following: hemoglobin level less than 9 g/dL in the presence of symptoms, or hemoglobin less than 7 g/dL without symptoms (*Lab should be drawn before transfusion or at least one month since last transfusion)

   AND
4. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Empaveli (pegcetacoplan) include: Patients with hypersensitivity to pegcetacoplan or any of the excipients, patients who are not currently vaccinated against certain encapsulated bacteria, Patients with unresolved serious infection caused by encapsulated bacteria]
   AND
5. Documentation member meets ONE of the following criteria: Thrombotic event(s) attributable to PNH (i.e. arterial/venous thrombosis, hepatic vein thrombosis, etc.) or major adverse vascular events from thromboembolism, Symptoms of PNH that inhibit the patient's quality of life (i.e. anemia, fatigue, difficulty swallowing, thromboses, frequent paroxysms of pain, recurrent abdominal pain, erectile dysfunction, chronic kidney disease, organ damage secondary to chronic hemolysis), OR Pregnant and potential benefit outweighs potential fetal risk

CONTINUATION OF THERAPY:
A. PAROXYSMAL NOCTURNAL HEMOGLOBINURIA:

1. Documentation of disease improvement or stabilization by any of the following: decrease in serum LDH, hemoglobin level above baseline, or reduction in the need for blood transfusions [DOCUMENTATION REQUIRED]
   AND
2. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
   AND
3. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity

DURATION OF APPROVAL:
Initial authorization: 6 months; Continuation of therapy: 12 months

PRESCRIBER REQUIREMENTS:
Prescribed by, or in consultation with, a board-certified hematologist, oncologist, immunologist, genetic specialist, or neurologist. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
18 years of age and older

QUANTITY:
1,080 mg twice weekly

Maximum Quantity Limits – 1,080 mg every three days for LDH level >2x the upper limit of normal (ULN)

PLACE OF ADMINISTRATION:
The recommendation is that SC infused medication in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Subcutaneous infusion

DRUG CLASS:
Complement Inhibitor

FDA-APPROVED USES:
Indicated for the treatment of adult patients with paroxysmal nocturnal hemoglobinuria (PNH).

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
PNH is a rare acquired clonal disorder caused by a somatic mutation of the phosphatidylinositol glycan-complementation class A (PIG-A) gene in hematopoietic stem cells. The disorder results in a deficiency of glycosylphosphatidylinositol (GPI), which serves as an anchor for several cell surface proteins including the terminal complement regulator, CD59. The absence of CD59 from the surface of the affected PNH red blood cells (RBCs) renders them susceptible to terminal complement- mediated lysis. The subsequent chronic hemolysis is the primary clinical manifestation of the disease and leads to disabling morbidities that include anemia, fatigue, thrombosis, pain, and impaired quality of life. Lactate dehydrogenase (LDH) is released during RBC destruction and grossly elevated serum LIH is a common finding in patients with PNH. Treatment includes supportive treatments (corticosteroids), treatment changing the course of the disease (eculizumab), and potential curative treatment (allogeneic bone marrow transplantation

Empaveli
Empaveli is the first targeted C3 complement inhibitor. It acts proximally in the complement cascade to control both intravascular and extravascular hemolysis, while Soliris and Ultomiris are effective in preventing intravascular hemolysis only. Extravascular hemolysis may contribute to the need for continued blood transfusions despite C5 inhibitor therapy.

Clinical Studies
NCT035005493- PEGASUS- Study to Evaluate the Efficacy and Safety of APL-2 in Patients With Paroxysmal Nocturnal Hemoglobinuria (PNH)

Study Population- Inclusion: Aged ≥18 years; primary diagnosis of PNH confirmed by high-sensitivity flow cytometry; ongoing treatment with stable dose eculizumab for ≥3 months; Hb <10.5 g/dL; absolute reticulocyte count >1.0 x ULN; platelet count of >50,000/mm3; ANC >500/mm3; BMI ≤35.0 kg/m2 Exclusion: Active bacterial infection not resolved within 14 weeks of study; receiving iron, folic acid, vitamin B12, or EPO, unless dose is stable, in 4 weeks prior to screening; hereditary complement deficiency; history of bone marrow transplantation; hypersensitivity or idiosyncratic reaction to compounds related to investigational product or subcutaneous administration; participation in any other investigational drug trial or exposure to other investigational agent within 30 days or 5 half-lives; breast-feeding women *Phase, Study Design, Sample Size*- Randomized, multicenter, open-label, active comparator-controlled study evaluating the safety and efficacy of APL-2 in patients with PNH N=80

Outcomes

APL-2 met the primary efficacy endpoint, demonstrating superiority to eculizumab with a statistically significant improvement in adjusted means of 3.8 g/dL of hemoglobin at Week 16 (P<0.0001) Pegcetacoplan-treated patients (n=41) had an adjusted mean Hb increase of 2.4 g/dL from a baseline of 8.7 g/dL, compared to eculizumab-treated patients (n=39) who had a change of −1.5 g/dL from a baseline of 8.7 g/dL at Week 16 7/41 patients (17.1%) in the pegcetacoplan group and 6/39 (15.4%) in the eculizumab group experienced an SAE. Most common AEs at 16 weeks in the pegcetacoplan and eculizumab groups were injection site reactions (36.6% vs 2.6%), diarrhea (22.0% vs 0%), headache (7.3% vs 20.5%), and fatigue (4.9% vs 15.4%) Hemolysis was reported in 4 patients in the pegcetacoplan group (9.8%) and 9 in the eculizumab group (23.1%), leading to 3 discontinuations in the pegcetacoplan group

Empaveli REMS

Because of the risk of serious infections, EMPAVELI is available only through a restricted program under a REMS. Under the EMPAVELI REMS, prescribers must enroll in the program.

Prescribers must counsel patients about the risk of serious infection, provide the patients with the REMS educational materials, and ensure patients are vaccinated against encapsulated bacteria.

Enrollment in the EMPAVELI REMS and additional information are available by telephone: 1-888-343-7073 or at www.empavelirems.com

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Empaveli (pegcetacoplan) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Empaveli (pegcetacoplan) include: Patients with 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.

OTHER SPECIAL CONSIDERATIONS:

Empaveli (pegcetacoplan) has a Black Box Warning for 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. Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for vaccinations against encapsulated bacteria. Vaccinate patients against encapsulated bacteria as recommended at least 2 weeks prior to administering the first dose of EMPAVELI unless the risks of delaying EMPAVELI therapy outweigh the risks of developing a serious infection. Vaccination reduces, but does not eliminate, the risk

of serious infections. Monitor patients for early signs of serious infections and evaluate immediately if infection is suspected. 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. Empaveli may interfere with laboratory tests: Use of silica reagents in coagulation panels may result in artificially prolonged activated partial thromboplastin time (aPTT).

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
N/A	

Related Administration Codes
96369: Sc Ther Infusion Up To 1 Hr
96371: Sc Ther Infusion Reset Pump

AVAILABLE DOSAGE FORMS:
Empaveli SOLN 1,080 mg/20 mL (54 mg/mL) in a single-dose vial

REFERENCES

1. Empaveli (pegcetacoplan) [prescribing information]. Waltham, MA: Apellis Pharmaceuticals Inc; February 2023.
2. Hillmen P, Szer J, Weitz I, et al. Pegcetacoplan versus eculizumab in paroxysmal nocturnal hemoglobinuria. N Engl J Med. 2021;384(11):1028-1037. doi:10.1056/NEJMoa2029073 [PubMed 33730455]
3. Hill A, et al. The incidence and prevalence of paroxysmal nocturnal hemoglobinuria (PNH) and survival of patients in Yorkshire. Blood. 2006; 108 (11):985. doi:10.1182/blood.V108.11.985.985
4. Peffault de Latour R, et al. Forty-Eight Week Efficacy and Safety of Pegcetacoplan in Adult Patients with Paroxysmal Nocturnal Hemoglobinuria and Suboptimal Response to Prior Eculizumab Treatment. Abstract S174. EHA 2021.
5. Apellis reports positive top-line results from phase 3 head-to-head study of pegcetacoplan (APL-2) compared to eculizumab in patients with paroxysmal nocturnal hemoglobinuria (PNH). News release. Apellis Pharmaceuticals, Inc.; January 7, 2020. https://investors.apellis.com/news-releases/news-release-details/apellis-reports-positive-top- line-results-phase-3-head-head.
6. Apellis Pharmaceuticals, Inc. Study to evaluate the efficacy and safety of APL-2 in patients with PNH. https://clinicaltrials.gov/ct2/show/NCT03500549. NLM identifier: NCT03500549.

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Products Affected Required Medical Information Prescriber Requirements Quantity Background References	Q3 2023
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Duration of Approval Prescriber Requirements Contraindications/Exclusions/Discontinuation Other Special Considerations	Q3 2022
Q2 2022 Established tracking in new format	Historical changes on file