Empaveli ™ (pegcetacoplan)
(Subcutaneous)

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I. Length of Authorization

- Coverage will be provided for 12 months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

– Empaveli 1,080 mg/20 mL solution in single-dose vials for infusion: 2 vials every 7 days

B. Max Units (per dose and over time) [HCPCS Unit]:

– 2,160 mg every 7 days

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Universal Criteria [1]

- Prescriber is enrolled in the Empaveli Risk Evaluation and Mitigation Strategy (REMS) program; **AND**
- Patient must be vaccinated against encapsulated bacteria (e.g., *Streptococcus pneumoniae, Neisseria meningitidis (serogroups A, C, W, Y and B), and Haemophilus influenzae type B*, etc.) according to current ACIP recommendations at least two weeks prior to initiation of therapy and will continue to be revaccinated in accordance with ACIP recommendations *(Note: If urgent Empaveli therapy is indicated in a patient who is not up to date according to ACIP recommendations, provide the patient with antibacterial drug prophylaxis and administer vaccine(s) as soon as possible)*; **AND**
- Patient does not have an unresolved, serious systemic infection from encapsulated bacteria (e.g., *Streptococcus pneumoniae, Neisseria meningitidis, and Haemophilus influenzae type B*, etc.); **AND**

- Will not be used in combination with another complement-inhibitor therapy (e.g., eculizumab, ravulizumab) *[Note: a 4-week run-in period is allowed when transitioning from eculizumab to pegcetacoplan – refer to Section V below]*; **AND**

Paroxysmal Nocturnal Hemoglobinuria (PNH) † Φ [1,4-7]

- Used as switch therapy*; **AND**
    - Patient is currently receiving treatment with Soliris or Ultomiris and has shown a beneficial disease response and absence of unacceptable toxicity while on therapy; **OR**
- Patient is complement inhibitor treatment-naïve*; **AND**
    - Diagnosis must be confirmed by detection of PNH clones of at least 10% by flow cytometry diagnostic testing; **AND**
    - Patient has the presence of at least 2 different glycosylphosphatidylinositol (GPI) protein deficiencies (e.g., CD55, CD59, etc.) within at least 2 different cell lines (e.g., granulocytes, monocytes, erythrocytes); **AND**
    - Patient has laboratory evidence of significant intravascular hemolysis (i.e., LDH ≥1.5 x ULN) with symptomatic disease and at least one other indication for therapy from the following (regardless of transfusion dependence):
        - Patient has symptomatic anemia (i.e., hemoglobin < 7 g/dL or hemoglobin < 10 g/dL, in at least two independent measurements in a patient with cardiac symptoms
        - Presence of a thrombotic event related to PNH
        - Presence of organ damage secondary to chronic hemolysis (i.e., renal insufficiency, pulmonary insufficiency/hypertension)
        - Patient is pregnant and potential benefit outweighs potential fetal risk
        - Patient has disabling fatigue
        - Patient has abdominal pain (requiring admission or opioid analgesia), dysphagia, or erectile dysfunction; **AND**
    - Documented baseline values for one or more of the following (necessary for renewal): serum lactate dehydrogenase (LDH), hemoglobin level, packed RBC transfusion requirement, history of thrombotic events

***Note:** All patients must initiate therapy at the lowest starting dosing/frequency (i.e., twice weekly infusions). For dose escalation requests (i.e., every 3 days), see Section IV.*

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1,6,7]

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria identified in section III; **AND**

- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: serious infections caused by encapsulated bacteria, severe infusion-related/hypersensitivity reactions (e.g., facial swelling, rash, urticaria, anaphylaxis), etc.; **AND**
- Patient has not developed severe bone marrow failure syndrome (i.e., aplastic anemia or myelodysplastic syndrome) OR experienced a spontaneous disease remission OR received curative allogeneic stem cell transplant; **AND**
    - Patient has shown a beneficial disease response compared to pretreatment baseline as indicated by one or more of the following:
        - Decrease in serum LDH
        - Stabilization/increase in hemoglobin level
        - Decrease in packed RBC transfusion requirement (i.e., reduction of at least 30%)
        - Reduction in thromboembolic events; **OR**
    - Dose escalation (up to the maximum dose and frequency specified below) may occur upon clinical review on a case by case basis provided that the patient has:
        - Shown an initial response to therapy; **AND**
        - Received initial dose and interval for at least 4 weeks, as specified below; **AND**
        - Patient lactate dehydrogenase (LDH) levels are greater than 2x the upper limit of normal (ULN) despite initial treatment

Switch therapy from Soliris or Ultomiris to Empaveli

- *Refer to Section III for criteria*

V. Dosage/Administration [1]

Indication	Dose
Paroxysmal Nocturnal Hemoglobinuria (PNH)	Treatment Naive: – The recommended dose of Empaveli is 1,080 mg by SC infusion twice weekly via a commercially available infusion pump with a reservoir of at least 20 mL or with Empaveli single-use, disposable on body injector. Switch Therapy from C5-inhibitors: – To reduce the risk of hemolysis with abrupt treatment discontinuation: o For patients switching from eculizumab, initiate Empaveli while continuing eculizumab at its current dose. After 4 weeks, discontinue eculizumab before continuing on monotherapy with Empaveli. o For patients switching from ravulizumab, initiate Empaveli no more than 4 weeks after the last dose of ravulizumab. Dose Adjustment – For lactate dehydrogenase (LDH) levels >2x the upper limit of normal, adjust the dosing regimen to 1,080 mg every three days. See Section IV for dose escalation criteria.

- *Empaveli is for subcutaneous administration using an infusion pump or Empaveli Injector, a single-use, disposable on body injector.*
- *Empaveli is intended for use under the guidance of a healthcare professional. After proper training on preparation and administration, a patient may self-administer, or the patient's caregiver may administer Empaveli, if a healthcare provider determines that it is appropriate.*
- *In the event of a dose increase, monitor LDH twice weekly for at least 4 weeks.*

VI. Billing Code/Availability Information

HCPCS Code(s):

- J7799 – Noc drugs, other than inhalation drugs, administered through dme (infusion pump)
- C9399 – Unclassified drugs or biologicals (Hospital-Outpatient Prospective Payer System Use Only-HOPPS)
- J3490 – Unclassified drugs

NDC:

- Empaveli 1,080 mg/20 mL solution in single-dose vials for infusion: 73606-0010-xx

VII. References

1. Empaveli [package insert]. Waltham, MA; Apellis Pharmaceuticals, Inc; February 2024. Accessed April 2024.
2. Guidelines for the diagnosis and monitoring of paroxysmal nocturnal hemoglobinuria and related disorders by flow cytometry. Borowitz MJ, Craig FE, DiGiuseppe JA, Illingworth AJ, Rosse W, Sutherland DR, Wittwer CT, Richards SJ. Cytometry B Clin Cytom. 2010 Jul;78(4):211-30. doi: 10.1002/cyto.b.20525.
3. Parker C, Omine M, Richards S, et al. Diagnosis and management of paroxysmal nocturnal hemoglobinuria. Blood. 2005 Dec 1. 106(12):3699-709.
4. Sahin F, Akay OM, Ayer M, et al. Pesg PNH diagnosis, follow-up and treatment guidelines. Am J Blood Res. 2016;6(2): 19-27.
5. Hillmen P, Szer J, Weitz I, et al. Pegcetacoplan versus Eculizumab in Paroxysmal Nocturnal Hemoglobinuria. N Engl J Med. 2021 Mar 18;384(11):1028-1037. doi: 10.1056/NEJMoa2029073.
6. Patriquin CJ, Kiss T, Caplan S, et al. How we treat paroxysmal nocturnal hemoglobinuria: A consensus statement of the Canadian PNH Network and review of the national registry. Eur J Haematol. 2019;102(1):36. Epub 2018 Oct 25.
7. Cançado RD, Araújo AdS, Sandes AF, et al. Consensus statement for diagnosis and treatment of paroxysmal nocturnal haemoglobinuria. Hematology, Transfusion and Cell Therapy, v43, Iss3, 2021, 341-348. ISSN 2531-1379, https://doi.org/10.1016/j.htct.2020.06.006.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
D59.5	Paroxysmal nocturnal hemoglobinuria [Marchiafava-Micheli]

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCA/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC