UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2025 P 2244-7
Program	Prior Authorization/Medical Necessity
Medication	Empaveli® (pegcetacoplan)
P&T Approval Date	7/2021, 7/2022, 8/2023, 2/2024, 4/2024, 4/2025, 10/2025
Effective Date	1/1/2026

1. Background

Empaveli (pegcetacoplan) is a complement inhibitor indicated for the treatment of adult patients with paroxysmal nocturnal hemoglobinuria (PNH) and 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.

2. Coverage Criteria[a]:

A. Paroxysmal Nocturnal Hemoglobinuria (PNH)

1. Initial Authorization

a. **Empaveli** will be approved based on **all** of the following criteria:

(1) Submission of medical records (e.g., chart notes, laboratory values, etc.) documenting the diagnosis of paroxysmal nocturnal hemoglobinuria (PNH) as confirmed by **both** of the following:

(a) Flow cytometry analysis confirming presence of PNH clones

-AND-

(b) Laboratory results, signs, and/or symptoms attributed to PNH (e.g., abdominal pain, anemia, dyspnea, extreme fatigue, smooth muscle dystonia, unexplained/unusual thrombosis, hemolysis/hemoglobinuria, kidney disease, pulmonary hypertension, etc.)

-AND-

(2) **One** of the following:

(a) Patient will not be prescribed Empaveli in combination with another complement inhibitor used for the treatment of PNH (e.g., Bkemv, Epysqli, Fabhalta, PiaSky, Soliris, Ultomiris)

-OR-

(b) Patient is currently receiving another complement inhibitor (e.g., Bkemv, Epysqli, Fabhalta, PiaSky, Soliris, Ultomiris) which will be discontinued and

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Empaveli will be initiated in accordance with the United States Food and Drug Administration approved labeling

-AND-

(3) Prescribed by, or in consultation with **one** of the following:

(a) Hematologist
(b) Oncologist

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Empaveli** will be approved based on **all** of the following criteria:

(1) Documentation of positive clinical response to Empaveli therapy (e.g., increased or stabilization of hemoglobin levels, reduction in transfusions, improvement in hemolysis, decrease in LDH, increased reticulocyte count, etc.)

-AND-

(2) Patient is not receiving Empaveli in combination with another complement inhibitor used for the treatment of PNH (e.g., Bkemv, Epysqli, Fabhalta, PiaSky, Soliris, Ultomiris)

-AND-

(3) Prescribed by, or in consultation with **one** of the following:

(a) Hematologist
(b) Oncologist

Authorization will be issued for 12 months.

B. C3 Glomerulopathy (C3G) or Primary Immune-Complex Membranoproliferative Glomerulonephritis (IC-MPGN)

1. **Initial Authorization**

a. **Empaveli** will be approved based on **all** of the following criteria:

(1) **One** of the following:

(a) **All** of the following:

i. Diagnosis of immune complex/monoclonal immunoglobulin-mediated Membranoproliferative glomerulonephritis (IC-MPGN)

-AND-

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ii. Confirmation of diagnosis is based on immunofluorescence microscopy on kidney biopsy

-AND-

iii. **All** of the following secondary causes of IC-MPGN have been ruled out:

- Infections (e.g., Hepatitis B and hepatitis C virus, chronic bacterial infections, parasitic infections)
- Autoimmune diseases [e.g., systemic lupus erythematosus (SLE), Sjogren's syndrome, rheumatoid arthritis, systemic sclerosis]
- Monoclonal gammopathy

-AND-

iv. Patient has not had a kidney transplant

-OR-

(b) **All** of the following:

i. Diagnosis of complement 3 glomerulopathy (C3G)

-AND-

ii. Confirmation of diagnosis is based on immunofluorescence microscopy on kidney biopsy

-AND-

iii. **One** of the following:

- Serum complement 3 (C3) protein < 77 mg/dL (alternatively, less than 0.85 x lower limit of the central laboratory normal range)

- Other complement abnormalities are present [e.g., soluble membrane attack complex (sC5b-9), serum factor H, serum factor B, factor I, membrane cofactor protein (MCP, CD46), C3/C4/C5 nephritic factor (NeF)] which are suggestive of a C3 glomerulopathy

-AND-

iv. Presence of monoclonal gammopathy of undetermined significance (MGUS) has been excluded by measurement of serum free light chains or other investigative means based on standards of care

-AND-

(2) Glomerulonephritis has persisted ≥ 3 months in duration

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-AND-

(3) Disease is considered to be moderate to severe based on proteinuria ≥ 1.5 g/day and/or abnormal kidney function

-AND-

(4) Used to reduce proteinuria

-AND-

(5) History of failure, contraindication or intolerance to a glucocorticoid (e.g., methylprednisolone, prednisone)

-AND-

(6) **One** of the following:

(a) Patient is on a stabilized dose and receiving concomitant therapy with **one** of the following:

i. Maximally tolerated angiotensin converting enzyme (ACE) inhibitor (e.g., captopril, enalapril)
ii. Maximally tolerated angiotensin II receptor blocker (ARB) (e.g., candesartan, valsartan)

-OR-

(b) Patient has an allergy, contraindication, or intolerance to ACE inhibitors and ARBs

-AND-

(7) Patient is not receiving Empaveli in combination with another complement inhibitor used for the treatment of C3G or IC-MPGN (e.g., Bkemv, Epysqli, Fabhalta, PiaSky, Soliris, Ultomiris)

-AND-

(8) Prescribed by or in consultation with a nephrologist

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Empaveli** will be approved based on **all** of the following criteria:

(1) Documentation of positive clinical response to Empaveli therapy demonstrated by a reduction in proteinuria

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-AND-

(2) Patient is not receiving Empaveli in combination with another complement inhibitor used for the treatment of C3G or IC-MPGN (e.g., Bkemv, Epysqli, Fabhalta, PiaSky, Soliris, Ultomiris)

-AND-

(3) Prescribed by or in consultation with a nephrologist

Authorization will be issued for 12 months.

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

3. Additional Clinical Rules:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply limits may be in place.

4. References:

1. Empaveli [package insert], Waltham, MA: Apellis Pharmaceuticals, Inc.; September 2023.
2. Parker C, Omine M, Richards S, et al. Diagnosis and management of paroxysmal nocturnal hemoglobinuria. Blood. 2005 Dec 1; 106(12): 3699–3709.
3. Devalet B, Mullier F, Chatelain B, et al. Pathophysiology, diagnosis, and treatment of paroxysmal nocturnal hemoglobinuria: a review. Eur J Haematol. 2015 Sep;95(3):190-8.
4. Sutherland DR, Keeney M, Illingworth A. Practical guidelines for the high-sensitivity detection and monitoring of paroxysmal nocturnal hemoglobinuria clones by flow cytometry. Cytometry B Clin Cytom. 2012 Jul;82(4):195-208.
5. Röth A, Maciejewski J, Nishimura JI, et al. Screening and diagnostic clinical algorithm for paroxysmal nocturnal hemoglobinuria: Expert consensus. Eur J Haematol. 2018 Jul;101(1):3-11.
6. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases. *Kidney Int*. 2021;100(4S):S1-S276. doi:10.1016/j.kint.2021.05.021
7. Fervenza, FC. Membranoproliferative glomerulonephritis: classification, clinical features, and diagnosis. In: UpToDate, Lam A (Ed), UpToDate, Waltham, MA, 2025.
8. Kopel, T. C3 glomerulopathies: Dense deposit disease and C3 glomerulonephritis. In: UpToDate, Lam, A (Ed), UpToDate, Waltham, MA, 2025.

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Program	Prior Authorization/Medical Necessity - Empaveli® (pegcetacoplan)
Change Control	
7/2021	New program
7/2022	Annual review with no changes to coverage criteria. Updated citations in background and coverage criteria.
8/2023	Annual review. Updated references.
2/2024	Added Fabhalta to list of examples of other complement inhibitors used for the treatment of PNH. Revised initial authorization to 12 months. Included criteria for therapeutic duplication. Updated references.
4/2024	Simplified criteria language for converting to new complement inhibitor therapy.
4/2025	Annual review. No changes to coverage criteria. Updated examples of alternate complement inhibitors.
10/2025	Added criteria for new FDA-approved indications C3G and IC-MPGN. Updated background and references.

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