Addendum to the Protocol for Paroxysmal Nocturnal Hemoglobinuria (PNH) Products
July 2025

DURB Approval Dates	**7/2022, 10/2024, 7/2025**
Commissioners Approval Dates	**3/2023, 1/2025**

Preferred Agents:
Epysqli (eculizumab)

Non-Preferred Agents:
Empaveli (pegcetacoplan)
Soliris (eculizumab)
Ultomiris (ravulizumab-cwvz)
Fabhalta (iptacopan)
PiaSky (crovalimab-akkz)
Voydeya (danicopan)
Bkemv (eculizumab)

Protocol applies to FDA approved biosimilars and related indications and dosages

Addendum:

The purpose of this addendum is to update the continuation of therapy criteria.

Background:

Paroxysmal nocturnal hemoglobinuria (PNH) is a chronic, multi-systemic, progressive, and life-threatening disease characterized by intravascular hemolysis, thrombotic events, serious infections, and bone marrow failure.

Empaveli is a complement inhibitor indicated for the treatment of adult patients with PNH.

Soliris and its biosimilars Bkemv and Epysqli are complement inhibitors indicated for the treatment of patients with PNH to reduce hemolysis.

Ultomiris is a complement inhibitor indicated for the treatment of pediatric and adult patients with PNH.

Fabhalta is a complement factor B inhibitor, indicated for the treatment of adults with PNH.

PiaSky is a complement C5 inhibitor indicated for the treatment of adult and pediatric patients 13 years and older with PNH and body weight of at least 40 kg

Voydeya is a complement factor D inhibitor indicated as an add-on therapy to ravulizumab or eculizumab for the treatment of extravascular hemolysis (EVH) in adults with PNH

Criteria for approval:

1. Diagnosis of PNH is confirmed by flow cytometry
2. Patient is of the FDA-labeled or compendial approved age
3. Patient does not have any FDA-labeled contraindications to requested medication
4. Patient is not on concomitant therapy with another complement inhibitor for the treatment of

PNH, unless indicated for add-on therapy

5. Patient complies with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for vaccinations against encapsulated bacteria
6. The medication requested is prescribed in accordance with a Food and Drug Administration (FDA) established indication and dosing regimens or in accordance with a medically appropriate off-label indication and dosing according to American Hospital Formulary Service, Micromedex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs (Lexicomp), national guidelines, or other peer-reviewed evidence
7. For Ultomiris and PiaSky requests patient's current weight is documented
8. For Fabhalta requests the medication is prescribed by or in consultation with a hematologist, oncologist, or immunologist
9. For Voydeya Requests:
    a. Patient has evidence of extravascular hemolysis while on a C5 inhibitor such as eculizumab, ravulizumab, or crovalimab
    b. Medication is used concomitantly with a C5 inhibitor
    c. Hemoglobin is ≤ 9.5 g/dL

NOTE: Empaveli, Soliris, Bkemv, Epysqli, Ultomiris, Fabhalta, PiaSky, Voydeya are available only through a restricted distribution program

Continuation of therapy:

1. The patient has responded to treatment compared to baseline as defined by at least ONE of the following:
    a. Decrease in serum LDH from pre-treatment level
    b. Increase in hemoglobin levels from pre-treatment level
    c. Decrease in number of transfusions needed
    d. Decrease in reticulocyte count from pre-treatment level
2. Patient is not on concomitant therapy with another complement inhibitor for the treatment of PNH, unless indicated for add-on therapy
3. The medication requested is prescribed in accordance with a Food and Drug
4. Administration (FDA)-established indication and dosing regimens or in accordance with a medically appropriate off-label indication and dosing according to American Hospital Formulary Service, Micromedex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs (Lexicomp), national guidelines, or other peer-reviewed evidence

Approval Duration and Quantity Limits:

Initial Approval: 6 months

Renewal Approval: 12 months

Quantity Level Limit: Reference Formulary for drug specific quantity level limits.

– Soliris, Epysqli, Bkemv (eculizumab) 600 mg IV once weekly for 4 weeks, then 900 mg IV once weekly for 1 week, and then 900 mg IV every 2 weeks.

- Fabhalta (iptacopan) 200mg capsules: 60 capsules per 30 days
- Piasky 340mg/2 mL (170mg/mL) single-dose vial: 2 single-dose vials per 28 days
- Ultomiris 245mg/3.5mL (70 mg/mL) single-dose prefilled cartridge for use only with supplied single-use on-body inj: 8 single-dose prefilled cartridges per 28 days
- Voydeya (danicopan) 150 mg dose carton (packaged as four 7-day blister cards containing 50 mg (21 tablets per card) and 100 mg tablets (21 tablets per card) [168 tablets per carton]): 1 carton (168 tablets) per 28 days.
- Voydeya (danicopan) 150 mg dose carton (packaged as 50 mg tablets (90 count bottle) and 100 mg tablets (90 count bottle) [180 tablets per carton]): 1 carton (180 tablets) per 30 days.
- Voydeya (danicopan) 200 mg dose carton (packaged as four 7-day blister cards containing 100 mg tablets (42 tablets per card) [168 tablets per carton]): 1 carton (168 tablets) per 28 days.
- Voydeya (danicopan) 200 mg dose carton (packaged as 100 mg tablets (two 90 count bottles) [180 tablets per carton]): 1 carton (180 tablets) per 30 days

References:

1. Empaveli® [prescribing information]. Apellis Pharmaceuticals Inc; Waltham MA. February 2024.
2. Soliris® [prescribing information]. Alexion Pharmaceuticals, Inc. Cheshire, CT. February 2025.
3. Ultomiris® [prescribing information]. Alexion Pharmaceuticals, Inc. Boston, MA. September 2024.
4. Fabhalta® [prescribing information]. Novartis Pharmaceuticals Corporation, East Hanover, NJ. March 2025.
5. PiaSky® [prescribing information]. Genentech, Inc. South Francisco, CA. June 2024.
6. Voydeya® [prescribing information]. Alexion Pharmaceuticals. Boston, MA. March 2024.
7. Clinical Pharmacology® Gold Standard Series [Internet database]. Tampa FL. Elsevier 2019. Updated periodically.
8. Cancado RD et al. Consensus statement for diagnosis and treatment of paroxysmal nocturnal hemoglobinuria. Hematol Transfus Cell Ther. 2021; 43(3):341-348.
9. Parker CJ. Update on the diagnosis and management of paroxysmal nocturnal hemoglobinuria. Hematology Am Soc Hematol Educ Program (2016) 2016 (1): 208–216.
10. Besa EC. Paroxysmal Nocturnal Hemoglobinuria Treatment & Management. Medscape. June 25, 2024. Accessed August 9, 2024, at: https://emedicine.medscape.com/article/207468-treatment?form=fpf
11. Cançado RD, Araújo ADS, Sandes AF, Arrais C, Lobo CLC, Figueiredo MS, Gualandro SFM, Saad STO, Costa FF. Consensus statement for diagnosis and treatment of paroxysmal nocturnal haemoglobinuria. Hematol Transfus Cell Ther. 2021 Jul-Sep;43(3):341-348. doi: 10.1016/j.htct.2020.06.006. Epub 2020 Jul 6. PMID: 32713742; PMCID: PMC8446255.
12. Makam AN, Suh K, Fahim SM, Carlson JJ, Herce-Hagiwara B, Richardson M, Dickerson R, Pearson SD, Agboola F. Iptacopan and Danicopan for Paroxysmal Nocturnal Hemoglobinuria: Effectiveness and Value; Evidence Report. Institute for Clinical and Economic Review, February 1, 2024. https://icer.org/assessment/paroxysmal-nocturnal-hemoglobinuria-2024/