Addendum to the Protocol for Paroxysmal Nocturnal Hemoglobinuria Products

Approved October 2024

Empaveli® (pegcetacoplan)
Soliris® (eculizumab)
Ultomiris® (ravulizumab)
Fabhalta® (iptacopan)
PiaSky® (crovalimab)
Voydeya® (danicopan)

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. The purpose of this addendum is to add new FDA-approved products, Fabhalta, PiaSky, and Voydeya.

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

Soliris *is a complement inhibitor 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. Medication 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

3. For Empaveli:
   a. Patient is 18 years old or older
   b. Prescriber is enrolled in Empaveli REMS program
   c. Patient will not be on concomitant therapy with another complement inhibitor such as Ultomiris or Soliris, unless otherwise recommended by the drug label
   d. Patient complies with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for vaccinations against encapsulated bacteria

4. For Soliris:
   a. Patient is 18 years of age or older
   b. Prescriber is enrolled in Soliris REMS program
   c. Patient will not be on concomitant therapy with another complement inhibitor such as Empaveli, PiaSky or Ultomiris unless otherwise recommended by drug label
   d. Patient complies with the most current ACIP recommendations for vaccinations against encapsulated bacteria

5. For Ultomiris:
   a. Patient is 1 month of age or older
   b. Prescriber is enrolled in Ultomiris REMS program
   c. Patient will not be on concomitant therapy with another complement inhibitor such as Empaveli, PiaSky or Soliris unless otherwise recommended by drug label
   d. Patient complies with the most current ACIP recommendations for vaccinations against encapsulated bacteria
   e. Patient's current weight is documented

6. For Fabhalta:
   a. Patient is 18 years of age or older
   b. Prescriber is enrolled in Fabhalta REMS program
   c. Medication is prescribed by or in consultation with a hematologist, oncologist, or immunologist
   d. Patient complies with the most current ACIP recommendations for vaccinations against encapsulated bacteria

7. For PiaSky:
   a. Patient is 13 years of age or older
   b. Prescriber is enrolled in PiaSky REMS program
   c. Patient will not be on concomitant therapy with another complement inhibitor such as Empaveli or Ultomiris, or Soliris unless otherwise recommended by drug label
   d. Patient complies with the most current ACIP recommendations for vaccinations against encapsulated bacteria
   e. Patient's current weight is documented

8. For Voydeya:
   a. Patient is 18 years of age or older
   b. Prescriber is enrolled in Voydeya REMS program
   c. Patient has evidence of extravascular hemolysis while on a C5 inhibitor such as eculizumab, ravulizumab, or crovalimab
   d. Medication will be used concomitantly with a C5 inhibitor
   e. Hemoglobin is ≤ 9.5 g/dL

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. Absence of unacceptable toxicity from the drug

Approval Duration and Quantity Restrictions:

Initial Approval: 6 months

Renewal Approval: 12 months

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

- 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: May 2021
2. Soliris [prescribing information]. Alexion Pharmaceuticals, Inc. Cheshire, CT: September 2011
3. Ultomiris [prescribing information]. Alexion Pharmaceuticals, Inc. Boston, MA: December 2018
4. Fabhalta [prescribing information]. Novartis Pharmaceuticals Corporation, East Hanover, NJ. August 2021
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
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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.