MED RX POLICY

POLICY: Complement Inhibitors – Paroxysmal Nocturnal Hemoglobinuria Med Rx Policy
- Bkemv™ (eculizumab-aeeb intravenous infusion – Amgen)
- PiaSky® (crovalimab-akkz intravenous infusion or subcutaneous injection – Genentech/Roche)
- Soliris® (eculizumab intravenous infusion – Alexion)
- Ultomiris® (ravulizumab-cwvz intravenous infusion – Alexion)

REVIEW DATE: 04/23/2025

OVERVIEW

Eculizumab (Soliris, biosimilars), Piasky, and Ultomiris are complement C5 inhibitors indicated for the treatment of **paroxysmal nocturnal hemoglobinuria** (PNH).[1-3] Both eculizumab and Ultomiris are indicated for use in other conditions.[2,3]

For PNH, Piasky is indicated for use in patients ≥ 13 years of age who weigh ≥ 40 kg; eculizumab is indicated for use in patients ≥ 18 years of age; and Ultomiris is indicated for use in patients ≥ 1 month of age.[1-3]

The dosing regimen for PiaSky consists of a loading dose, which consists of one intravenous (IV) infusion followed by four subcutaneous (SC) injections and the maintenance dose is given SC starting on Day 29 and every 4 weeks thereafter.[1] Both eculizumab and Ultomiris are given as IV infusions; the dose of Ultomiris is weight-based.[2,3]

Guidelines

There are no formal PNH guidelines. Consensus statements and expert opinion generally recommend a C5 inhibitor (eculizumab [Soliris, biosimilars], Ultomiris) for the treatment of symptomatic PNH.[4-7] A consensus statement for the diagnosis and treatment of PNH was published in 2021.[8] PiaSky is not mentioned in the consensus statements. Ultomiris is noted as an agent that is similar in efficacy and safety to eculizumab and due to the longer half-life, Ultomiris is administered once every 4 or 8 weeks (patients 5 to < 20 kg and patients ≥ 20 kg, respectively). The consensus statement notes that treatment options for PNH include supportive care (e.g., use of oral iron to replace large urinary losses; red blood cell transfusions [if needed] to maintain adequate hemoglobin levels), allogeneic hematopoietic stem cell transplantation, and complement blockade by the anti-C5 monoclonal antibody (eculizumab).

POLICY STATEMENT

This Med Rx program has been developed to encourage the use of Preferred Products. For all products (Preferred and Non-Preferred), the patient is required to meet the respective standard *Utilization Management Medical Policy* criteria. This program also directs the patient to try two Preferred Products (one eculizumab product and Ultomiris) prior to the approval of a Non-Preferred Product. Requests for the Non-Preferred Product will also be reviewed using the exception criteria (below). All approvals are provided for the duration noted in the respective *Complement Inhibitors Utilization Management Medical Policy*.

Documentation: Documentation is required for use of eculizumab (Soliris, Bkemv) and/or Ultomiris as noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to chart notes, prescription claims records, and prescription receipts.

Automation: None.

Preferred Products: Bkemv, Soliris, Ultomiris
Non-Preferred Product: PiaSky

RECOMMENDED EXCEPTION CRITERIA

Non-Preferred Product	Exception Criteria
PiaSky	**1. Paroxysmal Nocturnal Hemoglobinuria**. Approve if the patient meets BOTH of the following (A and B): **A)** Patient meets the *Complement Inhibitors – PiaSky Utilization Management Medical Policy* criteria; AND **B)** Patient meets ONE of the following (i, ii, iii, or iv): **i.** If patient is ≥ 18 years of age, patient meets BOTH of the following (a and b) **a)** Patient has tried one of Bkemv or Soliris **[documentation required]**; AND **b)** Patient has tried Ultomiris **[documentation required]**; OR **ii.** If patient is < 18 years of age, patient has tried Ultomiris **[documentation required]**; OR **iii.** Patient is unable to maintain intravenous (IV) access; OR **iv.** Patient is currently receiving PiaSky.

REFERENCES

1. PiaSky® [prescribing information]. South San Francisco, CA: Genentech; June 2024.
2. Soliris® intravenous infusion [prescribing information]. Boston, MA: Alexion; February 2025.
3. Ultomiris® [prescribing information]. Boston, MA: Alexion; September 2024.
4. Begum F, Khan N, Boisclair S, et al. Complement inhibitors in the management of complement-mediated hemolytic uremic syndrome and paroxysmal nocturnal hemoglobinuria. *Am J Ther*. 2021;30:e209-e219.
5. Szlendak U, Budziszewska B, Spychalska J, et al. Paroxysmal nocturnal hemoglobinuria: advances in the understanding of pathophysiology, diagnosis, and treatment. *Pol Arch Intern Med*. 2022;132(6):16271.
6. Waheed A, Shammo J, and Dingli D. Paroxysmal nocturnal hemoglobinuria: review of the patient experience and treatment landscape. *Blood Reviews*. 2024;64:101158.
7. Oliver M and Patriquin CJ. Paroxysmal nocturnal hemoglobinuria: current management, unmet needs, and recommendations. *J Blood Med*. 2023;14:613-628.
8. Cançado RD, da Silva Araújo A, Sandes AF, et al. Consensus statement for diagnosis and treatment of paroxysmal nocturnal haemoglobinuria. *Hematol Transfus Cell Ther*. 2021;43:341-348.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	Effective 01/01/2025.	11/13/2024
Early Annual Revision	**Paroxysmal Nocturnal Hemoglobinuria:** Bkemv, biosimilar to Soliris, is added to the list of Preferred Products. Previous exception criterion for a patient ≥ 18 years of age required a patient to have tried both Soliris and Ultomiris; the new criterion requires the patient to have tried one eculizumab product (either Bkemv or Soliris) and Ultomiris.	04/23/2025