UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Complement Inhibitors – PiaSky UM Medical Policy
- PiaSky® (crovalimab-akkz intravenous infusion or subcutaneous injection – Genentech)

REVIEW DATE: 05/21/2025

OVERVIEW

PiaSky, a complement C5 inhibitor, is indicated for the treatment of **paroxysmal nocturnal hemoglobinuria** (PNH) in patients ≥ 13 years of age who weigh ≥ 40 kg.[1]

Disease Overview

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, genetic disorder of hematopoietic stem cells.[2,3] The mutation in the X-linked gene phosphatidylinositol glycan class A (PIGA) results in a deficiency in the glycosylphosphatidylinositol (GPI) protein, which is responsible for anchoring other protein moieties to the surface of the erythrocytes. Loss of anchoring of these proteins causes cells to hemolyze and leads to complications such as hemolytic anemia, thrombosis, and peripheral blood cytopenias. PNH is a clinical diagnosis that should be confirmed with peripheral blood flow cytometry to detect the absence or severe deficiency of GPI-anchored proteins on at least two lineages.[2,5] Prior to the availability of complement inhibitors, only supportive management, in terms of managing the cytopenias and controlling thrombotic risk were available. Supportive measures include platelet transfusion, immunosuppressive therapy for patients with bone marrow failure, use of erythropoietin for anemias, and aggressive anticoagulation.

Dosing Information

The recommended dosage regimen for PiaSky consists of one loading dose administered by intravenous infusion on Day 1, followed by four weekly loading doses administered by subcutaneous (SC) injection on Days 2, 8, 15, and 22.[1] Maintenance doses start on Day 29 and are given once every 4 weeks by SC injection. Only healthcare providers should administer PiaSky.

Safety

PiaSky prescribing information has a Boxed Warning about serious meningococcal infections.[1] PiaSky is only available through a restricted access program, PiaSky Risk Evaluation and Mitigation Strategy (REMS).

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of PiaSky. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with PiaSky as well as the monitoring required for adverse events and long-term efficacy, approval requires PiaSky to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of PiaSky is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Paroxysmal Nocturnal Hemoglobinuria.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, and iv):
     - **i.** Patient is ≥ 13 years of age; AND
     - **ii.** Patient weighs ≥ 40 kg; AND
     - **iii.** Diagnosis was confirmed by peripheral blood flow cytometry results showing the absence or deficiency of glycosylphosphatidylinositol (GPI)-anchored proteins on at least two cell lineages; AND
     - **iv.** The medication is prescribed by or in consultation with a hematologist; OR
   - **B)** Patient is Currently Receiving PiaSky subcutaneous. Approve for 1 year if the patient meets ALL of the following (i, ii, iii, and iv):
     Note: A patient who has not started maintenance therapy with PiaSky subcutaneous should be considered under criterion A (Initial Therapy).
     - **i.** Patient is ≥ 13 years of age; AND
     - **ii.** Patient weighs ≥ 40 kg; AND
     - **iii.** According to the prescriber, patient is continuing to derive benefit from PiaSky; AND
       Note: Examples of benefit include increase in or stabilization of hemoglobin levels, decreased transfusion requirements or transfusion independence, reductions in hemolysis, improvement in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue score.
     - **iv.** The medication is prescribed by or in consultation with a hematologist.

   Dosing. Approve ONE of the following (A or B):
   - **A.** Initial Therapy. Approve ONE of the following (i or ii):
     - **i.** Patient weighs ≥ 40 kg to < 100 kg: Approve ALL of the following (a, b, and c):
       a) Loading dose on Day 1: 1,000 mg via intravenous infusion; AND
       b) Loading doses on Days 2, 8, 15, and 22: 340 mg via subcutaneous injection; AND
       c) Maintenance doses, starting on Day 29: 680 mg via subcutaneous injection once weekly every 4 weeks; OR
     - **ii.** Patient weighs ≥ 100 kg: Approve if the patient meets ALL of the following (a, b, and c):
       a) Loading dose on Day 1: 1,500 mg via intravenous infusion; AND
       b) Loading doses on Days 2, 8, 15, and 22: 340 mg via subcutaneous injection; AND
       c) Maintenance doses, starting on Day 29: 1,020 mg via subcutaneous injection once weekly every 4 weeks; OR
   - **B.** Patient is Currently Receiving PiaSky. Approve ONE of the following (i or ii):
     - **i.** Patient weighs ≥ 40 kg to < 100 kg: Approve maintenance dose of 680 mg administered via subcutaneous injection once every 4 weeks.
     - **ii.** Patient weighs ≥ 100 kg: Approve maintenance dose of 1,020 mg administered via subcutaneous injection once every 4 weeks.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of PiaSky is not recommended in the following situations:

1. **Concomitant Use with Another Complement Inhibitor**. There is no evidence to support concomitant use of PiaSky with another complement inhibitor.
   Note: Examples of complement inhibitors are Empaveli (pegcetacoplan subcutaneous injection), Fabhalta (iptacopan capsule), eculizumab intravenous infusion (Soliris, biosimilars), Ultomiris (ravulizumab cwzy intravenous infusion), Voydeya (danicopan tablets).

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. PiaSky® [prescribing information]. South San Francisco, CA: Genentech; June 2024.
2. 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.
3. Shah N, Bhatt H. Paroxysmal Nocturnal Hemoglobinuria. [Updated 2023 Jul 31]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK562292/. Accessed on May 13, 2025.
4. Roth A, Maciejewski J, Nishinura JI, et al. Screening and diagnostic clinical algorithm for paroxysmal nocturnal hemoglobinuria: Expert consensus. *Eur J Haematol*. 2018;101(1):3-11.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	07/10/2024
Early Annual Revision	**Paroxysmal Nocturnal Hemoglobinuria:** For patients who are currently receiving PiaSky, the Note regarding examples of benefit of PiaSky is updated to include "improvement in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue score". Dosing section was separated to provide dosing information for Initial Therapy and for a Patient who is Currently Receiving PiaSky. Previously the dosing section included information on loading doses and maintenance doses without separation. **Conditions Not Recommended for Approval:** Biosimilars to Soliris were added to the criteria where only Soliris was previously noted. Ultomiris subcutaneous injection was removed from criteria since the manufacturer has decided not to market the product.	05/21/2025