Drug Coverage Policy

Effective Date.....11/15/2024
Coverage Policy Number.....IP0694
Policy Title.....PiaSky

Complement Inhibitors – PiaSky

- PiaSky® (crovalimab-akkz intravenous infusion or subcutaneous injection – Genentech)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Cigna Healthcare Coverage Policy

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, which are given once every 4 weeks by SC injection, start on Day 29. Only healthcare providers should administer PiaSky.

Safety
The 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).

Medical Necessity Criteria

PiaSky is considered medically necessary when the following are met:

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, iv and v):
     - **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.
     - **v.** Preferred product criteria is met for the product(s) as listed in the below table(s)
   - **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.
     - **iv.** The medication is prescribed by or in consultation with a hematologist.

   Dosing. Approve ONE of the following weight-based regimens (A or B):

A. Patient weighs ≥ 40 kg to < 100 kg: Approve if the patient meets ALL of the following (i, ii, and iii):
- **i.** Loading dose on Day 1: 1,000 mg via intravenous infusion; AND
- **ii.** Loading doses on Days 2, 8, 15, and 22: 340 mg via subcutaneous injection; AND
- **iii.** Maintenance doses, starting on Day 29 and every 4 weeks thereafter: 680 mg via subcutaneous injection; OR

B. Patient weighs ≥ 100 kg: Approve if the patient meets ALL of the following (i, ii, and iii):
- **i.** Loading dose on Day 1: 1,500 mg via intravenous infusion; AND
- **ii.** Loading doses on Days 2, 8, 15, and 22: 340 mg via subcutaneous injection; AND
- **iii.** Maintenance doses, starting on Day 29 and every 4 weeks thereafter: 1,020 mg via subcutaneous injection.

Employer Plans:

Product	Criteria
PiaSky (crovalimab-akkz intravenous infusion or subcutaneous injection)	**ONE** of the following (1, 2, 3, or 4): 1. Patient has tried one of Soliris or Ultomiris 2. Patient < 18 years of age AND the patient has tried Ultomiris 3. Patient is unable to maintain intravenous access, approve. 4. Patient has already been started on therapy with PiaSky

Individual and Family Plans:

Product	Criteria
PiaSky (crovalimab-akkz intravenous infusion or subcutaneous injection)	**ONE** of the following (1, 2, 3, or 4): 1. Patient has tried one of Soliris or Ultomiris 2. Patient < 18 years of age AND the patient has tried Ultomiris 3. Patient is unable to maintain intravenous access, approve. 4. Patient has already been started on therapy with PiaSky

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

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), Soliris (eculizumab intravenous infusion), Ultomiris (ravulizumab cwzy intravenous infusion or subcutaneous injection), Voydeya (danicopan tablets).

Coding Information

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
C9399	Unclassified drugs or biologicals
J3590	Unclassified biologics

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 July 1, 2024.
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.

Revision Details

Type of Revision	Summary of Changes	Date
New	New policy	10/15/2024
Selected Revision	**Added** a preferred product step, through Soliris or Ultomiris, for both Employer Plans and Individual and Family Plans.	11/15/2024

The policy effective date is in force until updated or retired.