Drug Coverage Policy

Effective Date.....11/1/2025
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 where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. 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.

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).

Coverage Policy

POLICY STATEMENT
Prior Authorization is required for 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.

Documentation: Documentation is required where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory tests, claims records, and/or other information.

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 **[documentation required]**; AND
iv. The medication is prescribed by or in consultation with a hematologist; AND
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, 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.

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 1) an eculizumab product (Soliris, Bkemv, Epysqli) or 2) Ultomiris **[documentation required]** Note: All of the eculizumab products would count as one alternative (Soliris, Bkemv, Epysqli). 2. Patient < 18 years of age AND the patient has tried Ultomiris **[documentation required]** 3. Patient is unable to maintain intravenous access 4. Patient has already been started on therapy with PiaSky **[documentation required]**

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 1) an eculizumab product (Soliris, Bkemv, Epysqli) or 2) Ultomiris **[documentation required]** Note: All of the eculizumab products would count as one alternative (Soliris, Bkemv, Epysqli). 2. Patient < 18 years of age AND the patient has tried Ultomiris **[documentation required]** 3. Patient is unable to maintain intravenous access 4. Patient has already been started on therapy with PiaSky **[documentation required]**

Conditions Not Covered

PiaSky for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as newly 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), eculizumab intravenous infusion (Soliris, biosimilars), Ultomiris (ravulizumab cwzy intravenous infusion, Voydeya (danicopan tablets).

Coding Information

Note:
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 (Code effective until 12/31/2024)
J1307	Injection, crovalimab-akkz, 10 mg (Code effective 1/1/2025)
J3590	Unclassified biologics (Code effective until 12/31/2024)

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.

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
Selected Revision	**Updated HCPCS Coding:** **Added** J1307 (Code effective 1/1/2025) **Updated** the description for C9399 & J3590 to include the note "Code effective until 12/31/2024"	12/1/2024
Selected Revision	**Preferencing Table.** **Added** eculizumab product (Bkemv, Epysqli) **Added "**Note: All of the eculizumab products would count as one alternative (Soliris, Bkemv, Epysqli)."	7/1/2025
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. **Added** "documentation required" language to coverage policy criteria.	8/15/2025
Selected Revision	**Updated** policy template.	11/1/2025

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