## Clinical Policy: Crovalimab-akkz (PiaSky)

Reference Number: PA.CP.PHAR.664
Effective Date: 09/2024
Last Review Date: 07/2025

**Description**
Crovalimab (PiaSky®) is a complement C5 inhibitor.

**FDA Approved Indication(s)**
PiaSky is indicated for the treatment of adult and pediatric patients 13 years and older with paroxysmal nocturnal hemoglobinuria (PNH) and a body weight of at least 40 kg.

**Policy/Criteria**
*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of PA Health & Wellness® that PiaSky is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

**A. Paroxysmal Nocturnal Hemoglobinuria** (must meet all)**:**

1. Diagnosis of PNH;
2. Prescribed by or in consultation with a hematologist;
3. Age ≥ 13 years;
4. Body weight ≥ 40 kg;
5. Flow cytometry shows detectable glycosylphosphatidylinositol (GPI)-deficient hematopoietic clones or ≥ 10% PNH cells;
6. Failure of a ≥ 3-month trial of Soliris® or Ultomiris® up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization may be required for Soliris and Ultomiris*
7. PiaSky is not prescribed concurrently with another FDA-approved product for PNH (e.g., Bkemv™, Epysqli™, Soliris, Ultomiris, Empaveli®, Fabhalta®, Voydeya™);
8. Documentation of member's current body weight (in kg);
9. Dose does not exceed the following (a, b, c, and d):
   a. IV loading dose on Day 1 (i or ii):
      i. Weight ≥ 40 to < 100 kg: 1,000 mg;
      ii. Weight ≥ 100 kg: 1,500 mg;
   b. SC loading doses starting Day 2: 340 mg every week;
   c. SC maintenance doses starting Day 29 (i or ii):
      i. Weight ≥ 40 to < 100 kg: 680 mg every 4 weeks;
      ii. Weight ≥ 100 kg: 1,020 mg every 4 weeks;
   d. If member is switching therapy from Soliris/Bkemv/Epysqli or Ultomiris, administration of the IV loading dose should occur at the time of the next scheduled C5 inhibitor dose.

**Approval duration: 6 months**

**B. Other diagnoses/indications**
1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

## II. Continued Therapy

**A. Paroxysmal Nocturnal Hemoglobinuria** (must meet all)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in any of the following parameters (a – f):
    a. Improved measures of intravascular hemolysis (e.g., normalization of lactate dehydrogenase [LDH]);
    b. Reduced need for red blood cell transfusions;
    c. Increased or stabilization of hemoglobin levels;
    d. Less fatigue;
    e. Improved health-related quality of life;
    f. Fewer thrombotic events;
3. Documentation of member's current body weight (in kg);
4. PiaSky is not prescribed concurrently with another FDA-approved product for PNH (e.g., Bkemv, Epysqli, Soliris, Ultomiris, Empaveli, Fabhalta, Voydeya);
5. If request is for a dose increase, new dose does not exceed one of the following (a or b):
    a. Weight ≥ 40 to < 100 kg: 680 mg SC every 4 weeks;
    b. Weight ≥ 100 kg: 1,020 mg SC every 4 weeks.

**Approval duration: 12 months**

**B. Other diagnoses/indications** (must meet 1 or 2)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   **Approval duration: Duration of request or 12 months (whichever is less)**; or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

## III. Diagnoses/Indications for which coverage is NOT authorized:

**A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53

## IV. Appendices/General Information

*Appendix A: Abbreviation/Acronym Key*

FDA: Food and Drug Administration
GPI: glycosyl phosphatidylinositol
IV: intravenous
LDH: lactate dehydrogenase
PNH: paroxysmal nocturnal hemoglobinuria
SC: subcutaneous

*Appendix B: Therapeutic Alternatives*
*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.*

<table>
<tr><th>Drug Name</th><th>Dosing Regimen</th><th>Dose Limit/ Maximum Dose</th></tr>
<tr><td>Soliris (eculizumab)</td><td>IV infusion: 600 mg weekly for the first 4 weeks, followed by 900 mg for the fifth dose 1 week later, then 900 mg every 2 weeks thereafter</td><td>900 mg/dose</td></tr>
<tr><td>Ultomiris (ravulizumab-cwvz)</td><td>IV dosing:<br>Day 1: Loading dose IV<br>Day 15 and thereafter: Maintenance dose IV. If currently receiving SC Ultomiris, administer IV Ultomiris maintenance dose starting 1 week after last SC Ultomiris maintenance dose
<table>
<tr><th>Body Weight Range (kg)</th><th>Loading Dose (mg)</th><th>Maintenance Dose (mg)</th></tr>
<tr><td>≥ 5 to < 10</td><td>600</td><td>300 every 4 weeks</td></tr>
<tr><td>≥ 10 to < 20</td><td>600</td><td>600 every 4 weeks</td></tr>
<tr><td>≥ 20 to < 30</td><td>900</td><td>2,100 every 8 weeks</td></tr>
<tr><td>≥ 30 to < 40</td><td>1,200</td><td>2,700 every 8 weeks</td></tr>
<tr><td>≥ 40 to < 60</td><td>2,400</td><td>3,000 every 8 weeks</td></tr>
<tr><td>≥ 60 to < 100</td><td>2,700</td><td>3,300 every 8 weeks</td></tr>
<tr><td>≥ 100</td><td>3,000</td><td>3,600 every 8 weeks</td></tr>
</table>
SC dosing (maintenance only for age ≥ 18 years and weight ≥ 40 kg): 490 mg SC per week, starting 2 weeks after IV Ultomiris loading dose or 8 weeks after last IV Ultomiris maintenance dose</td><td>IV: 3,600 mg/ 8 weeks<br><br>SC: 490 mg/week</td></tr>
</table>

*Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.*

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s): unresolved serious *Neisseria meningitidis* infection, hypersensitivity to crovalimab or any of the excipients
- Boxed warning(s): serious meningococcal infections

## V. Dosage and Administration

| Indication | Dosing Regimen | Maximum Dose |
|---|---|---|
| PNH | **Body weight ≥ 40 kg to < 100 kg:**<br>Day 1: 1,000 mg IV<br>Day 2, 8, 15, and 22: 340 mg SC<br>Day 29 and every 4 weeks thereafter: 680 mg SC | See regimen |

| Indication | Dosing Regimen | Maximum Dose |
|---|---|---|
| | **Body weight ≥ 100 kg:**<br>Day 1: 1,500 mg IV<br>Day 2, 8, 15, and 22: 340 mg SC<br>Day 29 and every 4 weeks thereafter: 1,020 mg SC | |

## VI. Product Availability

Single-dose vial: 340 mg/2 mL

## VII. References

1. PiaSky Prescribing Information. South San Francisco, CA: Genentech, Inc.; June 2024. Available at: https://www.piasky.com/. Accessed May 1, 2025.
2. Parker C, Omine M, Richards S, et al. Diagnosis and management of paroxysmal nocturnal hemoglobinuria. Blood 2005; 106(12):3699-3709. doi:10.1182/blood-2005-04-1717.
3. Borowitz MJ, Craig FE, DiGiuseppe JA, et al. Guidelines for the diagnosis and monitoring of paroxysmal nocturnal hemoglobinuria and related disorders by flow cytometry. Cytometry Part B (Clinical Cytometry). 2010; 78B: 211–23
4. ClinicalTrials.gov. NCT04432584. A study evaluating the safety, pharmacokinetics, and efficacy of crovalimab versus eculizumab in participants with paroxysmal nocturnal hemoglobinuria (PNH) currently treated with complement inhibitors (COMMODORE 1). Available at: https://clinicaltrials.gov/study/NCT04432584. Accessed May 1, 2025.
5. ClinicalTrials.gov. NCT04434092. A phase III study evaluating the efficacy and safety of crovalimab versus eculizumab in participants with paroxysmal nocturnal hemoglobinuria (PNH) not previously treated with complement inhibitors. (COMMODORE 2). Available at: https://clinicaltrials.gov/study/NCT04434092. Accessed May 1, 2025.
6. ClinicalTrials.gov. NCT04654468. A study evaluating the efficacy, safety, pharmacokinetics and pharmacodynamics of crovalimab in participants with paroxysmal nocturnal hemoglobinuria (PNH) not previously treated with complement inhibition (COMMODORE 3). Available at: https://clinicaltrials.gov/study/NCT04654468. Accessed May 1, 2025.
7. Scheinberg P, Clé DV, Kim JS, et al. Phase 3 randomized COMMODORE 1 trial: Crovalimab versus eculizumab in complement inhibitor-experienced patients with paroxysmal nocturnal hemoglobinuria. Am J Hematol. 2024 Sep; 99(9): 1757-1767.
8. Röth A, He G, Tong H, et al. Phase 3 randomized COMMODORE 2 trial: Crovalimab versus eculizumab in patients with paroxysmal nocturnal hemoglobinuria naive to complement inhibition. Am J Hematol. 2024 Sep; 99(9): 1768-1777.

## Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

| HCPCS Codes | Description |
|---|---|
| J1307 | Injection, crovalimab-akkz, 10 mg |

| Reviews, Revisions, and Approvals | Date |
|---|---|
| Policy created | 08/2024 |
| 1Q 2025 annual review: no significant changes; for continued therapy added examples of improved extravascular hemolysis to demonstrate positive response to therapy; HCPCS code added [J1307] and removed codes [C9399, J3590]; references reviewed and updated. | 01/2025 |
| 3Q 2025 annual review: removed example of improved extravascular hemolysis to demonstrate positive response to therapy given PiaSky's mechanism of action; revised continued approval duration from 6 to 12 months as PNH is a chronic condition; references reviewed and updated. | 07/2025 |