09-J4000-95

Original Effective Date: 09/15/24

Reviewed: 05/14/25

Revised: 06/15/25

Subject: Crovalimab (Piasky) Injection

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Paroxysmal Nocturnal Hemoglobinuria (PNH) is an uncommon, life-threatening hemolytic anemia; the incidence of PNH ranges from 0.1 to 0.2 per 100,000 persons per year. PNH results from an acquired genetic deficiency in the cytolytic complement cascade that renders red blood cells (RBCs) susceptible to lysis. Chronic destruction of PNH RBCs by complement leads to serious morbidities. Increased hemolysis at night, hypothesized to result from decreased blood pH and activation of the complement system, leads to characteristic bloody morning urination. Excessive or persistent intravascular hemolysis in persons with PNH results in anemia, hemoglobinuria, and complications related to the presence of plasma-free hemoglobin (e.g., thrombosis, abdominal pain, dysphagia, erectile dysfunction, and pulmonary hypertension). Extravascular hemolysis in PNH can also occur and result in reticuloendothelial destruction in the liver and spleen. Complement inhibitors are used in the treatment of PNH to reduce hemolysis and transfusion requirements.

Crovalimab (Piasky) is a complement C5 inhibitor that prevents the formation of the membrane attack complex (MAC). This prevents terminal complement-mediated intravascular hemolysis. Crovalimab is Food and Drug Administration (FDA) approved for the treatment of adults and pediatric patients 13 years and older with paroxysmal nocturnal hemoglobinuria (PNH) and body weight of at least 40 kilograms.

The approval of crovalimab was based on an open-label, active-controlled trial in patients with PNH in patients not previously treated with a complement inhibitor. Subjects were included if they had an LDH level greater than or equal to two times the upper limit of normal (ULN) and at least one or more PNH-related sign or symptom in the past 3 months. Subjects were randomized to receive either crovalimab or eculizumab over a 24 week period. The primary efficacy endpoints were proportion of patients with hemolysis control and proportion with transfusion avoidance. Crovalimab was non-inferior to eculizumab in hemolysis control (79.3% versus 79%) and transfusion avoidance (65.7% versus 68.1%).

Secondary endpoints were similar between groups in the proportion of patients with breakthrough hemolysis (10.4% vs 14.5%), stabilization of hemoglobin (63.4% versus 60.9%), and clinical improvement in the FACIT-Fatigue score from baseline. The most common adverse reactions included infusion-related reaction, diarrhea, respiratory tract infection, viral infection, and Type III hypersensitivity reactions. Crovalimab has a Risk Evaluation and Mitigation Strategy (REMS) program due to the risk for serious meningococcal infection.

POSITION STATEMENT:

Initiation of crovalimab (Piasky) **meets the definition of medical necessity** when:

1. Paroxysmal Nocturnal Hemoglobinuria (PNH)
    a. Flow cytometry to confirm PNH in both red and white blood cells (with at least 5% granulocyte or monocyte clone size) – lab documentation must be provided
    b. **ONE** of the following:
        i. Member's lactate dehydrogenase (LDH) is elevated (i.e., 1.5 times greater than the upper limit of normal [ULN] as determined by the laboratory performing the test) and **ONE** of the following:
            1. Member's disease is transfusion-dependent evidenced by 2 or more transfusions in the 12 months prior to crovalimab initiation – documentation must be provided
            2. Member has a history of a major adverse vascular event (MAVE) from thromboembolism (e.g., myocardial infarction, cerebrovascular accident, deep vein thrombosis) – documentation must be provided
            3. Member has anemia with a hemoglobin less than the lower limit of normal – lab documentation must be provided
        ii. Member has been previously receiving eculizumab (Soliris, Epysqli, Bkemv), pegcetacoplan (Empaveli), ravulizumab (Ultomiris), or iptacopan (Fabhalta) for the treatment of PNH and is switching to crovalimab– documentation must be provided
    c. The member will not receive an additional complement inhibitor (danicopan, eculizumab and biosimilars, iptacopan, ravulizumab, or pegcetacoplan)[a]
    d. Member had an inadequate response to **TWO** of the following – documentation must be provided:
        i. pegcetacoplan (Empaveli)
        ii. ravulizumab (Ultomiris)
        iii. eculizumab (Epysqli)
    e. **ONE** of the following:
        i. Member has been vaccinated against meningococcal infection at least 2 weeks prior to therapy initiation
        ii. Member has been vaccinated against meningococcal infection less than 2 weeks prior to therapy initiation and will receive prophylactic antibiotics for at least 2 weeks following vaccination.

f. There is no evidence of an active meningococcal infection

g. The dose does not exceed the following schedule based on actual body weight:

   i. Weight 40 kg to less than 100 kg

      1. 1000 mg intravenous loading dose on day 1
      2. 340 mg subcutaneous on day 2, 8, 15, and 22
      3. 680 mg subcutaneous on day 29 and every 4 weeks thereafter

   ii. Weight greater than 100 kg

      1. 1500 mg intravenous loading dose on day 1
      2. 340 mg subcutaneous on day 2, 8, 15, and 22
      3. 1020 mg subcutaneous on day 29 and every 4 weeks thereafter

Approval duration: 6 months

Continuation of crovalimab **meets the definition of medical necessity** when **ALL** of the following are met:

1. Member has a history of beneficial response to crovalimab therapy for the treatment of paroxysmal nocturnal hemoglobinuria (PNH) - examples of beneficial response include decreased requirement for transfusions, stabilization of hemoglobin, reduction of LDH – lab documentation must be provided
2. The member has been previously approved for crovalimab in the treatment of PNH by Florida Blue or another health plan in the past 2 years, **OR** the member has previously met all indication-specific criteria for coverage
3. Member has been revaccinated against meningococcal infection according to current medical guidelines for vaccination while on crovalimab therapy
4. There is no evidence of an active meningococcal infection
5. The member will not receive an additional complement inhibitor (danicopan, eculizumab and biosimilars, iptacopan, ravulizumab, pegcetacoplan)[a]
6. The dose does not exceed the following based on actual body weight:

   i. Weight 40 kg to less than 100 kg: 680 mg subcutaneous every 4 weeks

   ii. Weight greater than 100 kg: 1020 mg subcutaneous every 4 weeks

Approval duration: 1 year

[a] When converting from eculizumab or ravulizumab, initiate crovalimab no sooner than the next scheduled dose of eculizumab or ravulizumab to avoid a Type III hypersensitivity reaction.

NOTE: Quest Diagnostics® can perform the Flow cytometry assay (PNH with FLAER) used in the diagnosis of PNH.

DOSAGE/ADMINISTRATION:

Crovalimab is FDA-approved for the treatment of paroxysmal nocturnal hemoglobinuria in adults and pediatric patients greater than 40 kg. The does not exceed the following schedule based on actual body weight:

1. Weight 40 kg to less than 100 kg
    - 1000 mg intravenous loading dose on day 1
    - 340 mg subcutaneous on day 2, 8, 15, and 22
    - 680 mg subcutaneous on day 29 and every 4 weeks thereafter
2. Weight greater than 100 kg
    - 1500 mg intravenous loading dose on day 1
    - 340 mg subcutaneous on day 2, 8, 15, and 22
    - 1020 mg subcutaneous on day 29 and every 4 weeks thereafter

See prescribing information for converting from other complement inhibitors and for missing doses.

PRECAUTIONS:

Boxed warning:

Crovalimab increases the risk of serious and life-threatening meningococcal infections. Immunize members with a meningococcal vaccine at least 2 weeks prior to administering the first dose of crovalimab, unless the risks of delaying crovalimab therapy outweigh the risks of developing a meningococcal infection. Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in persons with complement deficiencies. Monitor members for early signs of meningococcal infections and evaluate immediately if infection is suspected. Crovalimab is only available through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS).

Contraindications:

- Do not initiate during unresolved serious Neisseria meningitidis infection
- Patients with a known serious hypersensitivity to crovalimab or any of the excipients

Precautions:

- Type III hypersensitivity reactions: Monitor patients switching between C5 inhibitors due to risk of Type III hypersensitivity reactions related to the formation of drug-target-drug complexes.
- May increase susceptibility to serious infections caused by encapsulated bacteria.
- Infusion and injection-related reactions: monitor for these reactions and initiate medical management as needed.

Availability:

340 mg/2mL single dose vial

BILLING/CODING INFORMATION:

HCPCS Coding

J1307	Injection, crovalimab-akkz, 10 mg

ICD-10 Diagnosis Codes That Support Medical Necessity

D59.5	Paroxysmal nocturnal hemoglobinuria [Marchiafava-Micheli]

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request

DEFINITIONS:

Paroxysmal nocturnal hemoglobinuria (PNH): A chronic acquired blood cell dysplasia with proliferation of a clone of stem cells producing erythrocytes, platelets, and granulocytes that are abnormally susceptible to lysis by complement; it is marked by episodes of intravascular hemolysis, causing hemolytic anemia, particularly following infections, and by venous thromboses, especially of the hepatic veins.

RELATED GUIDELINES:

Danicopan (Voydeya), 09-J4000-88

Iptacopan (Fabhalta), 09-J4000-80

Pegcetacoplan (Empaveli), 09-J4000-04

Eculizumab (Soliris), 09-J1000-17

Ravulizumab (Ultomiris), 09-J3000-26

OTHER:

None

REFERENCES:

1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2025. URL www.clinicalpharmacilogy-ip.com Accessed 05/01/25
2. Hui L, Xia L, Weng J et al. Efficacy and safety of the C5 inhibitor crovalimab in complement inhibitor-naïve patients with PNH (COMMODORE 3): A multicenter, Phase 3, single-arm study. *Am J Hematol*. 2023 Sep;98(9):1407 - 1414.
3. Micromedex® Healthcare Series [database online]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed 05/01/25
4. Piasky (crovalimab) [package insert]. Genentech, Inc. South San Francisco (CA): June 2024.
5. Roth A, He G, Tong H, et al. Phase 3 randomized COMMODORE 2 trial: Crovalimab versus eculizumab in patients with paroxysmal nocturnal hemoglobinuria naïve to complement inhibition. Am J Hematol. 2024 Jun 17.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 05/14/25.

GUIDELINE UPDATE INFORMATION:

09/15/24	New medical coverage guideline.
12/15/24	Review and revision to guideline; consisting of updating the position statement for paroxysmal nocturnal hemoglobinuria.
01/01/25	Revision: Added HCPCS code 1307 and deleted code J3590.
06/15/25	Review and revision to guideline; consisting of updating the step in the position statement for paroxysmal nocturnal hemoglobinuria.