Piasky ™ (crovalimab-akkz)
(Intravenous/Subcutaneous)

Document Number: EOCCO-0762

Last Review Date: 08/01/2024
Date of Origin: 08/01/2024
Dates Reviewed: 08/2024

I. Length of Authorization

- Coverage will be provided for 12 months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

– Piasky 340 mg/2 mL solution in single-dose vials for infusion:

Loading Dose: Five (5) vials on day 1 followed by one (1) vial on days 2, 8, 15, 22.

Maintenance Dose: Three (3) vials on day 29 and every 4 weeks thereafter

B. Max Units (per dose and over time) [HCPCS Unit]:

a. Loading Dose: 1,500 mg IV on day 1 followed by 340 mg SQ on days 2, 8, 15, 22.

b. Maintenance Dose: 1020 mg SQ on day 29 and every 4 weeks thereafter

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 13 years of age; **AND**

Universal Criteria [1]

- Patient body weight is at least 40 kg; **AND**
- Prescriber is enrolled in the Piasky Risk Evaluation and Mitigation Strategy (PIASKY REMS) program; **AND**
- Patient must be vaccinated against encapsulated bacteria (e.g., *Streptococcus pneumoniae, Neisseria meningitidis (serogroups A, C, W, Y and B), and Haemophilus influenzae type B, etc.)* according to current ACIP recommendations at least two weeks prior to initiation of therapy and will continue to be revaccinated in accordance with ACIP recommendations *(Note: If urgent Piasky therapy is indicated in a patient who is not up to date with vaccinations according to ACIP recommendations, provide the patient with antibacterial drug prophylaxis and administer vaccine(s) as soon as possible)*; **AND**

- Patient does not have an unresolved, serious systemic infection from encapsulated bacteria (e.g., *Streptococcus pneumoniae, Neisseria meningitidis, and Haemophilus influenzae type B, etc.)*; **AND**
- Will not be used in combination with another complement-inhibitor therapy (e.g., eculizumab, ravulizumab, pegcetacoplan, iptacopan) *[Note: switch therapy is allowed when transitioning from eculizumab or ravulizumab to crovalimab – refer to Section V below]*; **AND**

Paroxysmal Nocturnal Hemoglobinuria (PNH) † Φ [1,4-7]

- Used as switch therapy*; **AND**
    - Patient is currently receiving treatment with eculizumab or ravulizumab and has shown a beneficial disease response and absence of unacceptable toxicity while on therapy; **OR**
- Patient is complement inhibitor treatment-naïve*; **AND**
    - Diagnosis must be confirmed by detection of PNH clones of at least 10% by flow cytometry diagnostic testing; **AND**
    - Patient has the presence of at least 2 different glycosylphosphatidylinositol (GPI) protein deficiencies (e.g., CD55, CD59, etc.) within at least 2 different cell lines (e.g., granulocytes, monocytes, erythrocytes); **AND**
    - Patient has laboratory evidence of significant intravascular hemolysis (i.e., LDH ≥1.5 x ULN) with symptomatic disease and at least one other indication for therapy from the following (regardless of transfusion dependence):
        - Patient has symptomatic anemia (i.e., hemoglobin < 7 g/dL or hemoglobin < 10 g/dL, in at least two independent measurements in a patient with cardiac symptoms
        - Presence of a thrombotic event related to PNH
        - Presence of organ damage secondary to chronic hemolysis (i.e., renal insufficiency, pulmonary insufficiency/hypertension)
        - Patient is pregnant and potential benefit outweighs potential fetal risk
        - Patient has disabling fatigue
        - Patient has abdominal pain (requiring admission or opioid analgesia), dysphagia, or erectile dysfunction; **AND**
    - Documented baseline values for one or more of the following (necessary for renewal): serum lactate dehydrogenase (LDH), hemoglobin level, packed RBC transfusion requirement, history of thrombotic events

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1,6,7]

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: serious infections (especially those caused by encapsulated bacteria), severe infusion-related/hypersensitivity reactions (e.g., facial swelling, rash, urticaria, anaphylaxis), etc.; **AND**
- Patient has not developed severe bone marrow failure syndrome (i.e., aplastic anemia or myelodysplastic syndrome) OR experienced a spontaneous disease remission OR received curative allogeneic stem cell transplant; **AND**
    - Patient has shown a beneficial disease response compared to pretreatment baseline as indicated by one or more of the following:
        - Decrease in serum LDH
        - Stabilization/increase in hemoglobin level
        - Decrease in packed RBC transfusion requirement (i.e., reduction of at least 30%)
        - Reduction in thromboembolic events

Switch therapy from Eculizumab or Ravulizumab

- *Refer to Section III for criteria*

V. Dosage/Administration [1]

Indication	Dose
Paroxysmal Nocturnal Hemoglobinuria (PNH)	The recommended dosage regimen consists of one loading dose administered by intravenous (IV) infusion (on Day 1), followed by four additional weekly loading doses administered by subcutaneous (SUBQ) injection (on Days 2, 8, 15, and 22). The maintenance dose starts on Day 29 and is then administered every 4 weeks by subcutaneous injection. Administer doses based on the patient's actual body weight. – **Weight ≥ 40 kg to <100 kg** • Loading Dose: 1,000 mg IV on day 1 followed by 340 mg SQ on days 2, 8, 15, 22. • Maintenance Dose: 680 mg SQ on day 29 and every 4 weeks thereafter – **Weight ≥ 100 kg** • Loading Dose: 1,500 mg IV on day 1 followed by 340 mg SQ on days 2, 8, 15, 22. • Maintenance Dose: 1020 mg SQ on day 29 and every 4 weeks thereafter Switch Therapy from C5-inhibitors: – Healthcare providers should consider the benefits of the timing of switching C5 inhibitors vs. the risks of Type III hypersensitivity reactions. For patients switching from another C5 inhibitor (e.g.,

	eculizumab or ravulizumab), the first intravenous loading dose of Piasky should be administered no sooner than the time of the next scheduled complement inhibitor administration. The administration of the additional subcutaneous loading doses and maintenance doses of Piasky should follow as per the schedule shown above.
– *Piasky is administered as an intravenous infusion and subcutaneous injection (subsequent doses) that is administered by healthcare providers ONLY.*	

VI. Billing Code/Availability Information

HCPCS Code(s):

- J3590 – Unclassified biologic drugs

NDC:

- Piasky 340 mg/2 mL solution in single-dose vials for infusion: 50242-0115-xx

VII. References

1. Piasky [package insert]. San Francisco, CA; Genentech, Inc; June 2024. Accessed June 2024.
2. Guidelines for the diagnosis and monitoring of paroxysmal nocturnal hemoglobinuria and related disorders by flow cytometry. Borowitz MJ, Craig FE, DiGiuseppe JA, Illingworth AJ, Rosse W, Sutherland DR, Wittwer CT, Richards SJ. Cytometry B Clin Cytom. 2010 Jul;78(4):211-30. doi: 10.1002/cyto.b.20525.
3. Parker C, Omine M, Richards S, et al. Diagnosis and management of paroxysmal nocturnal hemoglobinuria. Blood. 2005 Dec 1. 106(12):3699-709.
4. Sahin F, Akay OM, Ayer M, et al. Pesg PNH diagnosis, follow-up and treatment guidelines. Am J Blood Res. 2016;6(2): 19-27.
5. Hillmen P, Szer J, Weitz I, et al. Pegcetacoplan versus Eculizumab in Paroxysmal Nocturnal Hemoglobinuria. N Engl J Med. 2021 Mar 18;384(11):1028-1037. doi: 10.1056/NEJMoa2029073.
6. Patriquin CJ, Kiss T, Caplan S, et al. How we treat paroxysmal nocturnal hemoglobinuria: A consensus statement of the Canadian PNH Network and review of the national registry. Eur J Haematol. 2019;102(1):36. Epub 2018 Oct 25.
7. Cançado RD, Araújo AdS, Sandes AF, et al. Consensus statement for diagnosis and treatment of paroxysmal nocturnal haemoglobinuria. Hematology, Transfusion and Cell Therapy, v43, Iss3, 2021, 341-348. ISSN 2531-1379, https://doi.org/10.1016/j.htct.2020.06.006.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
D59.5	Paroxysmal nocturnal hemoglobinuria [Marchiafava-Micheli]

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCA/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC