Medical Policy Bulletin

Title:
Crovalimab-akkz (PiaSky)
Policy #:
MA08.0178

The Company makes decisions on coverage based on the Centers for Medicare and Medicaid Services (CMS) regulations and guidance, benefit plan documents and contracts, and the member's medical history and condition. If CMS does not have a position addressing a service, the Company makes decisions based on Company Policy Bulletins. Benefits may vary based on contract, and individual member benefits must be verified. The Company determines medical necessity only if the benefit exists and no contract exclusions are applicable. Although the Medicare Advantage Policy Bulletin is consistent with Medicare's regulations and guidance, the Company's payment methodology may differ from Medicare.

When services can be administered in various settings, the Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition. This decision is based on the member's current medical condition and any required monitoring or additional services that may coincide with the delivery of this service.

This Policy Bulletin document describes the status of CMS coverage, medical terminology, and/or benefit plan documents and contracts at the time the document was developed. This Policy Bulletin will be reviewed regularly and be updated as Medicare changes their regulations and guidance, scientific and medical literature becomes available, and/or the benefit plan documents and/or contracts are changed.

Policy

Coverage is subject to the terms, conditions, and limitations of the member's Evidence of Coverage.

In the absence of coverage criteria from applicable Medicare statutes, regulations, NCDs, LCDs, CMS manuals, or other Medicare coverage documents, this policy uses internal coverage criteria developed by the Company in consideration of peer-reviewed medical literature, clinical practice guidelines, and/or regulatory status.

The Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition.

MEDICALLY NECESSARY

PAROXYSMAL NOCTURNAL HEMOGLOBINURIA (PNH)

Crovalimab-akkz (PiaSky) is considered medically necessary and, therefore, covered for the treatment of PNH in adult and pediatric (13 years and older) individuals, when all of the following criteria are met, including dosing and frequency:

Initial Criteria

- The individual has body weight 40 kg or more
- Flow cytometry demonstrates one of the following:
    - At least 10% PNH type III red cells
    - Greater than 50% of glycosylphosphatidylinositol-anchored proteins (GPI-AP)–deficient polymorphonuclear (PM) cells
- The individual exhibits clinical manifestations of disease (e.g., lactate dehydrogenase [LDH] greater than 1.5 upper limit of normal [ULN], thrombosis, renal dysfunction, pulmonary hypertension, dysphagia)
- The individual is transfusion dependent due to PNH.
- The individual does not have unresolved *Neisseria meningitidis* infection.
- The individual is vaccinated against *N. meningitidis,* unless risk of delaying crovalimab-akkz (PiaSky) outweighs the risks of developing meningococcal infection.

- Crovalimab-akkz (PiaSky) will not be used in combination with another complement inhibitor (e.g., Empaveli, Fabhalta, Soliris, Ultomiris) for the treatment of PNH.

- Dosing and frequency for crovalimab-akkz (PiaSky)
    - 40 kg to less than 100 kg: Loading dosage, 1000 mg IV on Day 1 followed by 340 mg subQ once weekly on Days 2, 8, 15, and 22
    - 40 kg to less than 100 kg: Maintenance dosage, 680 mg subQ starting on Day 29 and administered every 4 weeks thereafter
    - 100 kg or greater: Loading dosage, 1500 mg IV on Day 1 followed by 340 mg subQ once weekly on Days 2, 8, 15 and 22
    - 100 kg or greater: Maintenance dosage, 1020 mg subQ starting on Day 29 and administered every 4 weeks thereafter

Continuation Criteria

Crovalimab-akkz (PiaSky) is considered medically necessary and, therefore, covered for continuation therapy, when documentation is provided of positive clinical response (e.g., reduction in hemolysis manifested by stabilization of hemoglobin levels and reduction in transfusions from baseline at initiation).

EXPERIMENTAL/INVESTIGATIONAL

All other uses for crovalimab-akkz (PiaSky) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

DOSING AND FREQUENCY REQUIREMENTS

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this policy to ensure consistency with the most recently published recommendations for the use of crovalimab-akkz (PiaSky). Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to: the US Food and Drug Administration (FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of crovalimab-akkz (PiaSky) outside of the Dosing and Frequency Requirements listed in this policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the utilization management activities. The Company reserves the right to conduct postpayment review and audit procedures for any claims submitted for crovalimab-akkz (PiaSky).

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Guidelines

DRUG INFORMATION

Per the US Food and Drug Administration (FDA)–approved labeling, the recommended dosing and frequency of crovalimab-akkz (PiaSky) require loading dose(s) and maintenance doses based on body weight of the individual.

BLACK BOX WARNINGS

Refer to the specific manufacturer's prescribing information for any applicable Black Box Warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, crovalimab-akkz (PiaSky) is covered under the medical benefits of the Company's products when the medical necessity criteria including dosing and frequency requirements listed in this medical policy are met.

ON

PiaSky (crovalimab-akkz) was approved by the FDA in June 2024 for the treatment of adult and pediatric individuals 13 years and older with paroxysmal nocturnal hemoglobinuria (PNH) and body weight of at least 40 kg.
Dosing and frequency for crovalimab-akkz (PiaSky):

- 40 kg to less than 100 kg: Loading dosage, 1000 mg IV on Day 1 followed by 340 mg subQ once weekly on Days 2, 8, 15 and 22
- 40 kg to less than 100 kg: Maintenance dosage, 680 mg subQ starting on Day 29 and administered every 4 weeks thereafter
- 100 kg or greater: Loading dosage, 1500 mg IV on Day 1 followed by 340 mg subQ once weekly on Days 2, 8, 15 and 22
- 100 kg or greater: Maintenance dosage, 1020 mg subQ starting on Day 29 and administered every 4 weeks thereafter

PEDIATRIC USE

Use of crovalimab-akkz (PiaSky) in PNH: the safety and effectiveness have been established in the pediatric population 13 years of age and older.

Description

Crovalimab-akkz (PiaSky) is a C5 inhibitor that is recycled within the bloodstream and binds with high affinity to the complement protein C5, inhibiting its cleavage into C5a and C5b and preventing the formation of the membrane attack complex (MAC). This action inhibits terminal complement-mediated intravascular hemolysis in patients with paroxysmal nocturnal hemoglobinuria (PNH), delivering rapid and sustained complement inhibition. The US Food and Drug Administration (FDA) accepted a biologics license application for crovalimab-akkz (PiaSky) in September 2023, leading to its approval in June 2024 for the treatment of PNH in adult and adolescent individuals aged 13 years and older.

PAROXYSMAL NOCTURNAL HEMOGLOBINURIA (PNH)

PNH is a rare condition caused by genetic mutation in the production of red blood cells (RBCs). The mutation causes RBCs to form without terminal complement inhibitors. The absence of complement inhibitors leads to the constant premature destruction and loss of RBCs (hemolysis) by the individual's own immune system. The premature loss of RBCs can result in anemia, fatigue, difficulty in functioning, dark urine, pain, shortness of breath, and blood clots. Crovalimab-akkz (PiaSky) inhibits RBC mutation and prevents intravascular hemolysis.

RISK EVALUATION AND MITIGATION STRATEGY

Crovalimab-akkz (PiaSky) was approved by the FDA with a risk evaluation and mitigation strategy (REMS) due to the risk of meningococcal infections. Under the REMS, prescribers must enroll in the program, counsel individuals about the risk of meningococcal infection, provide individuals with the REMS educational materials, and ensure that individuals are vaccinated with a meningococcal vaccine.

OFF-LABEL INDICATIONS

There may be additional indications contained in the policy section of this document due to evaluation of criteria

highlighted in the company's off-label policy, and/or review of clinical guidelines issued by leading professional organizations and government entities.

PEER REVIEWED LITERATURE

The efficacy of crovalimab-akkz (PiaSky) was evaluated in an active-controlled, open-label, non-inferiority study COMMODORE 2 (NCT04434092) in individuals with PNH. A total of 204 individuals (body weight ≥40 kg) with PNH not previously treated with a complement inhibitor in a 2:1 ratio were randomly assigned to receive either crovalimab-akkz (PiaSky) (n=135) or eculizumab (Soliris) (n=69). The study additionally enrolled six pediatric individuals (aged >12 years and body weight ≥40 kg) to receive crovalimab-akkz (PiaSky) in a separate nonrandomized cohort. The primary efficacy objective of the study was to assess the noninferiority of crovalimab-akkz (PiaSky) compared with eculizumab (Soliris) with respect to the co-primary endpoints of hemolysis control and transfusion avoidance. Secondary endpoints were the proportion of individuals with breakthrough hemolysis (BTH) from baseline through week 25, the proportion of individuals with stabilized hemoglobin from baseline through week 25, and mean change from baseline to week 25 in fatigue assessed in adult individuals aged 18 years or older.

A single intravenous loading dose of crovalimab-akkz (PiaSky) was given on Day 1 (1000 mg for individuals weighing ≥40 kg to <100 kg, or 1500 mg for individuals weighing >100 kg), followed by four additional weekly subcutaneous loading doses of 340 mg on Days 2, 8, 15, and 22. Starting at Day 29, maintenance subcutaneous doses were given every 4 weeks (680 mg for individuals weighing ≥40 kg to <100 kg, or 1020 mg for individuals weighing ≥100 kg). The study consisted of a primary treatment period of 24 weeks, after which individuals had the option to continue or switch to crovalimab-akkz (PiaSky) in an extension period. Eligible individuals had LDH level 2 upper limit of normal (ULN) and at least one or more PNH-related signs or symptoms in the past three months. Randomization was stratified by the most recent lactate dehydrogenase (LDH) value (≥2 to ≤4 × ULN, or >4 × ULN) and by the transfusion history (0, >0 to ≤6, or >6 packed red blood cell [pRBC] units administered within 6 months prior to randomization). Crovalimab-akkz (PiaSky) was noninferior to eculizumab (Soliris) for both co-primary endpoints of hemolysis control and transfusion avoidance. The mean proportion of individuals with hemolysis control was 79.3% with crovalimab-akkz (PiaSky) and 79.0% with eculizumab (Soliris) . Crovalimab-akkz (PiaSky) was also non-inferior to eculizumab (Soliris) for the secondary endpoints of break-through hemolysis (BTH) and hemoglobin stabilization.The most common infusion-related reaction symptoms were headache (13.3%) and abdominal pain (1.5%) for crovalimab-akkz (PiaSky), and headache (8.7%) for eculizumab (Soliris).

References

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Coding

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

CPT Procedure Code Number(s)
N/A

ICD - 10 Procedure Code Number(s)
N/A

ICD - 10 Diagnosis Code Number(s)
D59.5 Paroxysmal nocturnal hemoglobinuria [Marchiafava-Micheli]

HCPCS Level II Code Number(s)
J1307 Injection, crovalimab-akkz, 10 mg

Revenue Code Number(s)
N/A

Policy History

Revisions From MA08.178:

09/16/2025	

	This new policy will become effective on 09/16/2025. The policy has been developed to communicate the Company's coverage position for crovalimab-akkz (PiaSky).

Version Effective Date:
09/16/2025
Version Issued Date:
N/A
Version Reissued Date:
N/A