09-J4000-67

Original Effective Date: 11/15/23

Reviewed: 10/11/23

Revised: 04/01/24

Subject: Pozelimab-bbfg (Veopoz)

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.

Dosage/ Administration	Position Statement	Billing/Coding	Reimbursement	Program Exceptions	Definitions
Related Guidelines	Other	References	Updates		

DESCRIPTION:

Complement hyperactivation, angiopathic thrombosis and protein-losing enteropathy (CHAPLE), or CD55-deficient PLE, is an ultra-rare and life-threatening autosomal recessive disorder that is driven by overactivation of the complement system. Mutations in the CD55 gene result in an inability to regulate complement activity and the complement system may attack normal cells causing damage to blood and lymph vessels along the upper digestive tract and leading to a loss of circulating proteins.CHAPLE disease typically manifests as peripheral and visceral edema due to severe hypoalbuminemia, diarrhea, abdominal pain, hypogammaglobulinemia, malabsorption, and malnutrition. Severe thrombotic vascular occlusions can also occur among patients with CHAPLE disease. Fewer than 100 patients worldwide and fewer than 10 patients in the United States are known to have CHAPLE disease.

On August 18, 2023, the U.S. Food and Drug Administration (FDA) approved Regeneron's Veopoz (pozelimab-bbfg) for the treatment of adult and pediatric patients 1 year of age and older with CHAPLE disease. This is the first FDA-approved treatment for this indication. Veopoz is an immunoglobulin G4 (IgG4) antibody that binds with high affinity to wild-type and variant human C5 protein thereby blocking the activity of complement factor C5 to prevent diseases mediated by the complement system. Prior to the approval of pozelimab-bbfg (Veopoz), there were no FDA-approved therapies for CHAPLE disease. Supportive interventions include albumin infusions, IgG replacement therapy, corticosteroids, bowel resection surgery, and vitamin and micronutrient supplements. None of these interventions are curative nor do they lead to lasting improvement. Additionally, eculizumab (Soliris), a complement C5 inhibitor, has been used off-label to treat CHAPLE disease.

The safety and efficacy of Veopoz were evaluated in a Phase 2/3 open-label, single-arm study (NCT04209634), in which outcomes were compared to pre-treatment data in patients with active CHAPLE disease who had hypoalbuminemia. The diagnosis of CHAPLE disease was based on a clinical

history of PLE symptoms and confirmed genotype of biallelic CD55 loss-of-function mutation. Participants received a single loading dose of Veopoz 30 mg/kg via IV infusion on day 1, followed by a once-weekly, weight-based maintenance dosage of SC Veopoz starting 1 week after the loading dose. Standard of care therapy (e.g., corticosteroids) were permitted, however use of other complement inhibitors was not allowed.

The primary endpoint was proportion of patients with active disease at baseline achieving both normalization of serum albumin and improvement on clinical outcomes (i.e. frequency of problematic abdominal pain, bowel movement frequency, facial and peripheral edema severity) who were evaluable for improvement at baseline, or proportion of patients with no worsening of clinical outcomes (if not evaluable for improvement at baseline), at week 24. Key secondary endpoints included incidence and severity of adverse events, albumin transfusions, serum IgG concentrations, and hospitalizations.

At 24 weeks, the co-primary endpoints were achieved, with 100% of patients experiencing normalization of serum albumin and improvement or no worsening of clinical symptoms. The median time for serum albumin to reach ≥3.5 g/dL was 15.5 days (N = 10; 95% CI: 8 to 28). All 10 patients achieved normalization of serum albumin concentrations by week 12 and maintained serum albumin concentrations within the normal range through at least 72 weeks of treatment. Analyses of secondary endpoints also demonstrated reductions in hospitalization days and total number of albumin transfusions, as well as increases in body weight for age and stature for age. The most common adverse reactions (in two or more patients) were upper respiratory tract infection, fracture, urticaria, and alopecia. The label for Veopoz carries a Boxed Warning regarding life-threatening and fatal meningococcal infections. Meningococcal vaccination should be completed or updated at least 2 weeks prior to administering the first dose of Veopoz unless the risks of delaying therapy outweigh the risks of developing meningococcal infection.

POSITION STATEMENT:

Initiation of pozelimab-bbfg (Veopoz) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Member is diagnosed with CD55-deficient protein-losing enteropathy (PLE)/complement hyperactivation, angiopathic thrombosis and protein-losing enteropathy (CHAPLE) disease (based on a history of PLE) – documentation from the medical record must be provided
2. Member's diagnosis is confirmed by biallelic CD55 loss-of-function mutation detected by genotype analysis – laboratory testing must be provided
3. Pozelimab-bbfg is prescribed by (or in consultation with) a gastroenterologist, hematologist, or a provider specializing in rare, genetic diseases
4. Member is not receiving treatment with another complement inhibitor (such as, eculizumab (Soliris) or ravulizumab (Ultomiris)) or the complement inhibitor will be discontinued upon initiation of pozelimab-bbfg
5. Dose does not exceed:
    a. Initiation: 30 mg/kg IV infusion x 1 dose
    b. Maintenance: 12 mg/kg SQ once weekly

6. Member is one year of age or older

Approval duration: 1 year

Continuation of pozelimab-bbfg (Veopoz) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Authorization/reauthorization has been previously approved by Florida Blue or another health plan (evidence of paid claim or prior approval must be submitted) in the past two years for treatment of CD-55 deficient PLE/CHAPLE disease, **OR** the member has previously met all indication-specific criteria
2. Member demonstrates a positive clinical response (such as, improvement or no worsening in clinical symptoms, increase in or stabilization of albumin and IgG concentrations, increase in growth percentiles) to treatment with pozelimab-bbfg – documentation from the medical record must be provided
3. Pozelimab-bbfg is prescribed by (or in consultation with) a gastroenterologist, hematologist, or a provider specializing in rare, genetic diseases
4. Member is not receiving treatment with another complement inhibitor (such as, eculizumab (Soliris) or ravulizumab (Ultomiris)) or the complement inhibitor will be discontinued upon initiation of pozelimab-bbfg
5. Dose does not exceed 12 mg/kg SQ once weekly

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Day 1 (Loading Dose):
  - Administer a single 30 mg/kg dose by intravenous infusion after dilution
  - Intravenous use must be prepared and administered by a healthcare provider
- Day 8 and Thereafter (Maintenance Dosage):
  - Inject 10 mg/kg as a subcutaneous injection once weekly starting on Day 8
  - The maintenance dosage may be increased to 12 mg/kg once weekly if there is inadequate clinical response after at least 3 weekly doses (i.e., starting from Week 4)
  - The maximum maintenance dosage is 800 mg once weekly
  - Doses greater than 400 mg require 2 injections.
  - Subcutaneous use must be prepared and administered by a healthcare provider

Dose Adjustments

- None

Drug Availability

- Injection: 400 mg/2 mL (200 mg/mL) in a single-dose vial

PRECAUTIONS:

Boxed Warning

- Life-threatening and fatal meningococcal infections have occurred in patients treated with complement inhibitors. Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early.
- Complete or update meningococcal vaccination at least 2 weeks prior to administering the first dose, unless the risks of delaying therapy outweigh the risks of developing meningococcal infection. Follow the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in patients receiving a complement inhibitor.
- Patients at increased risk for invasive disease caused by N. meningitidis, even if they develop antibodies following vaccination. Monitor patients for early signs of meningococcal infections and evaluate immediately if infection is suspected.

Contraindications

- Patients with unresolved Neisseria meningitidis infection

Precautions/Warnings

- Other Bacterial Infections: Interrupt treatment in patients who are undergoing treatment for a serious encapsulated bacterial infection until the infection is resolved.
- Systemic Hypersensitivity Reactions: Interrupt infusion and institute appropriate supportive measures if signs of cardiovascular instability or respiratory comprise occur.
- Immune Complex Formation: Transition between other complement inhibitors has resulted in decreased drug concentrations and possible hypersensitivity reactions.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J9376	Injection, pozelimab-bbfg, 1 mg

ICD-10 Diagnosis Codes That Support Medical Necessity

K90.49	Malabsorption due to intolerance, not elsewhere classified
D84.1	Defects in the complement system

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.

DEFINITIONS:

None

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

1. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2023 [cited 10/1/23]. Available from: http://www.clinicalpharmacology.com/.
2. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine; 2000 Feb 29 - [cited 10/1/23]. Available from: http://clinicaltrials.gov/.
3. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 10/1/23].
4. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2019 [cited 10/1/23]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.
5. Regeneron. Veopoz (pozelimab-bbfg). 2023 [cited 10/1/23]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=a8d6f10e-9430-450a-a3dd-b538f9b2a308.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 10/11/23.

GUIDELINE UPDATE INFORMATION:

11/15/23	New Medical Coverage Guideline.

04/01/24	Revision: Added HCPCS code J9376 and deleted code J3590.