pozelimab-bbfg (Veopoz™)

Medicare Advantage Medical Policy #MNG-065
Original Effective Date: 02/01/2025
Current Effective Date: 02/01/2025

Applies to all products administered or underwritten by the Health Plan, unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Health Plan may consider pozelimab-bbfg (Veopoz™)‡ for the treatment of CD55-deficient protein-losing enteropathy (PLE), also known as CHAPLE disease to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for pozelimab-bbfg (Veopoz) will be considered when the following criteria are met:

- Initial authorization (6 months):
  - Patient is 1 year of age or older; AND
  - Patient has a diagnosis of CD55-deficient protein-losing enteropathy (PLE), also known as CHAPLE disease; AND
  - Diagnosis has been verified by each of the following:
    - Documentation is provided showing biallelic CD55 loss-of-function mutation detected by genetic testing; AND
    - Documentation is provided showing hypoalbuminemia (defined as serum albumin concentration of ≤3.2 g/dL); AND
  - Documentation of active disease by one or more of the following signs or symptoms within the last six months:
    - Abdominal pain; OR
    - Diarrhea; OR
    - Peripheral edema; OR
    - Facial edema; AND
  - Patient has received vaccination against meningococcal infections at least 2 weeks prior to administering the first dose; OR, if the drug is initiated <2 weeks after meningococcal vaccination, patient will receive prophylactic antibiotics; AND
  - Patient does not have a history of meningococcal infection; AND
  - Requested medication is NOT used in combination with another complement inhibitor (such as, eculizumab (Soliris™)‡ or ravulizumab (Ultomiris™)‡), or the complement inhibitor will be discontinued upon initiation of the requested medication; AND

    - Maintenance dose does not exceed 800 mg subcutaneously once a week following the initial loading dose which does not to exceed 30 mg/kg IV infusion.
- Continuation:
  - Patient has received an initial authorization for Veopoz from the plan OR has provided documentation of authorization from previous Medicare Advantage plan; AND
    - Patient has experienced improvement while on therapy; such examples may include:
      - Increased serum albumin levels; OR
      - Maintenance of serum albumin levels within a normal range; OR
      - A reduction in albumin transfusions; OR
      - Increases in or maintenance of protein and/or immunoglobulin levels; OR
      - Improvement in clinical outcomes after receipt of therapy (e.g., decreases in the frequency of problematic abdominal pain, bowel movement frequency, facial edema severity, and peripheral edema severity); OR
      - Reduced frequency in hospitalizations; OR
      - Increase in growth percentiles (e.g., body weight-for age and/or stature-for-age percentiles); AND
    - Requested medication is NOT used in combination with another complement inhibitor (such as, eculizumab (Soliris) or ravulizumab (Ultomiris)), or the complement inhibitor will be discontinued upon initiation of the requested medication; AND
    - Dose does not exceed 800mg subcutaneously once a weekly.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Health Plan considers the use of pozelimab-bbfg (Veopoz) when ANY of the following criteria listed below are NOT met to be **not medically necessary****:

- For Initial Requests:
  - Documentation is provided showing hypoalbuminemia (defined as serum albumin concentration of ≤3.2 g/dL)
  - Documentation of active disease by one or more of the following signs or symptoms within the last six months:
    - Abdominal pain
    - Diarrhea
    - Peripheral edema
    - Facial edema
  - Patient does not have a history of meningococcal infection
- For continuation requests:
  - Patient has experienced improvement while on therapy; such examples may include:
    - Increased serum albumin levels
    - Maintenance of serum albumin levels within a normal range

- A reduction in albumin transfusions
- Increases in or maintenance of protein and/or immunoglobulin levels
- Improvement in clinical outcomes after receipt of therapy (e.g., decreases in the frequency of problematic abdominal pain, bowel movement frequency, facial edema severity, and peripheral edema severity)
- Reduced frequency in hospitalizations
- Increase in growth percentiles (e.g., body weight-for age and/or stature-for-age percentiles)

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Health Plan considers the use of pozelimab-bbfg (Veopoz) when the patient selection criteria are not met (EXCEPT those denoted above as **not medically necessary****) to be **investigational.***

Background/Overview

Veopoz is a complement inhibitor, indicated for the treatment of adult and pediatric patients 1 year of age and older with CD55-deficient protein-losing enteropathy (PLE), also known as CHAPLE disease. As the first FDA approved therapy for CHAPLE disease, Veopoz is a monoclonal antibody that targets complement factor C5, a protein involved in complement system activation. Because life threatening and fatal meningococcal infections have occurred in patients treated with complement inhibitors, patients must receive or update vaccination against meningococcal infection according to the most current Advisory Committee on Immunization Practices (ACIP) recommendations at least 2 weeks prior to the first dose of Veopoz. If vaccination cannot be given at least two weeks prior to the start of therapy, the package insert recommends that patients should receive prophylactic antibiotics. Veopoz requires a weight-based intravenous loading dose, followed by a weight-based subcutaneous dose on day 8, and then weekly subcutaneous maintenance doses thereafter. The maintenance dosage may be increased once weekly if there is inadequate clinical response after at least 3 weekly doses. The maximum maintenance dosage is 800 mg subcutaneously once a week.

CHAPLE Disease (CD55-deficient protein-losing enteropathy (PLE))

Complement hyperactivation, angiopathic thrombosis, and protein-losing enteropathy (CHAPLE) disease is a rare but life-threatening immune condition caused by a biallelic loss-of-function mutation in the *CD55* gene. *CD55* inhibits early complement activation by accelerating the degradation of C3 convertase, a key regulator of the complement cascade, and blocking cleavage of C5 into C5a and C5b, thereby preventing the formation of the membrane-attack complex (C5b-C9, a structure mediating cell lysis). The mutation at *CD55* allows overactivation of the complement system causing damage to blood and lymph vessels along the upper digestive tract and leading to a loss of circulating proteins. Patients may experience abdominal pain, diarrhea, vomiting, malabsorption, edema, delayed growth, intestinal lymphangiectasia, infections, and potentially life-

threatening thrombotic vascular occlusions. Onset occurs in infancy or childhood with approximately 10 patients in the US and 100 patients worldwide being affected by the disease.

There are no other FDA-approved therapies for CHAPLE disease. Soliris has been used off-label. Supportive therapies include albumin infusions, IgG replacement therapy, corticosteroids, bowel resection surgery, and vitamin and micronutrient supplements.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Veopoz was approved in August 2023 for the treatment of adult and pediatric patients 1 year of age and older with CD55-deficient protein-losing enteropathy (PLE), also known as CHAPLE disease.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of VEOPOZ was evaluated in one open-label, single-arm, multinational controlled, Phase II/III pivotal study where outcomes were compared to pre-treatment data in ten patients with active CD55-deficient protein-losing enteropathy (PLE) and hypoalbuminemia. Diagnosis was based on a clinical history of PLE and a confirmed genotype of biallelic CD55 loss-of-function mutation. Active CD55-deficient PLE was defined as hypoalbuminemia (serum albumin concentration of ≤3.2 g/dL) with one or more of the following signs or symptoms within the last six months: abdominal pain, diarrhea, peripheral edema, or facial edema. The median patient age was 8.5 years (range 3 to 19 years), and the mean baseline serum albumin concentration was 2.2 g/dL (range 1.1 to 2.9 g/dL). The primary endpoint was the proportion of patients achieving serum albumin normalization with improvement or no worsening in clinical outcomes (frequency of problematic abdominal pain, bowel movement frequency, facial edema severity, and peripheral edema severity) at Week 24. Patients received a single 30 mg/kg loading dose of Veopoz intravenous infusion over approximately one hour, followed by a once weekly weight-tiered maintenance dosage, administered as a subcutaneous injection starting one week after the loading dose. All patients received meningococcal vaccination prior to treatment with Veopoz and antibacterials for prophylaxis of meningococcal infection. Patients were permitted to receive additional therapies as part of standard of care, and use of other complement inhibitors was prohibited. The median time for serum albumin to reach at least 3.5 g/dL was 15.5 days with all 10 patients achieving normalization by Week 12 and maintaining serum albumin concentrations within the normal range through at least 72 weeks of treatment; symptomatic improvement was also noted. Five of the 10 patients received a total of 60 transfusions in the 48 weeks prior to treatment. In the 48 weeks after

commencing treatment, one patient received one albumin transfusion. Nine of the 10 patients were hospitalized for a total of 268 days in the 48 weeks prior to treatment. In the 48 weeks after starting therapy, two patients were hospitalized for a total of 7 days. Serum immunoglobulin G (IgG) concentrations reached normal values for age in all patients within the first 12 weeks of treatment with improvement maintained through at least 72 weeks of treatment.

References

1. Dho SH, et al. Beyond the Role of CD55 as a Complement Component. Immune Netw. 2018; 20;18(1):e11.
2. Veopoz Drug Evaluation. Express Scripts. Updated September 2023.
3. Veopoz [package insert]. Regeneron Pharmaceuticals, Inc. Tarrytown, NY. October 2023
4. Veopoz New Drug Review. IPD Analytics. Updated September 2023.

Policy History

Original Effective Date: 02/01/2025
Current Effective Date: 02/01/2025
11/19/2024 UM Committee review. New policy
Next Scheduled Review Date: 11/2025

Coding

The five character codes included in the Health Plan Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2023 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of the Health Plan Medical Policy Coverage Guidelines is with the Health Plan and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in the Health Plan Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of the Health Plan Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	C9399, J3590, J9376
ICD-10 Diagnosis	All related diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

NOTICE: If the Patient's health insurance contract contains language that differs from the Health Plan Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Health Plan recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

Medicare Advantage Members

Established coverage criteria for Medicare Advantage members can be found in Medicare coverage guidelines in statutes, regulations, National Coverage Determinations (NCD)s, and Local Coverage Determinations (LCD)s. To determine if a National or Local Coverage Determination addresses coverage for a specific service, refer to the Medicare Coverage Database at the following link: https://www.cms.gov/medicare-coverage-database/search.aspx. You may wish to review the Guide to the MCD Search here: https://www.cms.gov/medicare-coverage-database/help/mcd-bene-help.aspx.

When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, internal coverage criteria may be developed. This policy is to serve as the summary of evidence, a list of resources and an explanation of the rationale that supports the adoption of this internal coverage criteria.