Veopoz (pozelimab-bbfg)
PAM – 086

Iowa Medicaid Program	Prior Authorization	**Effective Date**	04/01/2024
Revision Number	1	**Last Reviewed**	10/18/2024
Reviewed By	Medicaid Medical Director	**Next Review**	04/18/2025
Approved By	Medicaid Clinical Advisory Committee	**Approved Date**	10/18/2024

Overview

Medication: [1]	pozelimab-bbfg	
Brand Name:	Veopoz®	
Pharmacologic Category:	Immunological Agent; complement inhibitor	
FDA-Approved Indication(s):	Treatment of adult and pediatric patients 1 year of age and older with CD55-deficient protein-losing enteropathy (PLE), also known as CHAPLE* disease *__C__omplement __H__yperactivation, __A__ngiopathic thrombosis, and __P__rotein-__L__osing __E__nteropathy	
How Supplied:	Single-dose vial containing 400 mg/2 mL (200 mg/mL)	
Dosage and Administration:	Loading Dose	30 mg/kg on Day 1 [intravenous (IV) infusion]
	Maintenance Dose	10 mg/kg once weekly [subcutaneous (SC) injection] starting on Day 8 • May be increased to 12 mg/kg once weekly if inadequate clinical response after at least 3 weekly doses (i.e., starting from week 4) • Maximum maintenance dosage is 800 mg once weekly • Doses greater than 400 mg require 2 injections • Must be prepared and administered by a healthcare provider
Benefit Category:	Medical	

WARNING – SERIOUS MENINGOCOCCAL INFECTIONS

- 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 (for serogroups A, C, W and Y, and serogroup B) at least 2 weeks prior to administering the first dose of Veopoz®, unless the risks of delaying therapy outweigh the risk of developing a meningococcal infection. Follow the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in patients receiving a complement inhibitor.
- Patients receiving Veopoz® are 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.

Descriptive Narrative

The complement system is a cascade of proteins that are important components of innate and adaptive immune responses to destroy pathogens and clear immune complexes, apoptotic cells, and debris. Complement activation produces bioactive peptides and anaphylatoxins, that can lead to the assembly of a membrane attack complex (MAC) that lyse targets such as pathogens or cells. Unwanted complement activation is regulated by the cell surface glycoproteins such as CD55 (also called decay accelerating factor [DAF]), CD46, and CD59, which protect normal hematopoietic, endothelial, and epithelial cells from complement-mediated damage. CD55 is a negative regulator of the C3 and C5 convertases that mediate cleavage activation of C3 and C5 and control activation of MAC; absence of functioning CD55 results in hyperactivation of the MAC and cell injury leading to manifestation of disease.

In CHAPLE disease (**C**omplement **H**yperactivation, **A**ngiopathic thrombosis, and **P**rotein-**L**osing **E**nteropathy), the terminal complement system (MAC) is unregulated/uninhibited due to the absence of CD55 on the cell surface; this specifically renders intestinal lymphatic endothelial cells vulnerable to inflammatory attack by the complement and innate immune overactivation. Diagnosis of CHAPLE disease is made by genetic testing "confirmed by biallelic CD55 loss-of-function mutation detected by genotype analysis (frameshift, nonsense mutations)." In the case of missense or suspected splice site mutations, CD55-deficient PLE can be confirmed by flow cytometry of peripheral blood cells or western blot. In addition, subjects with active CHAPLE disease are required to have clinical signs and symptoms of PLE.

CHAPLE disease is a rare disease, with fewer than 10 patients identified in the U.S., and fewer than 100 patients diagnosed worldwide. Symptoms can include abdominal pain, nausea, vomiting, diarrhea, loss of appetite, weight loss, impaired growth, and edema. Severe thrombotic vascular occlusions can also occur among patients with CHAPLE disease, which can be life-threating. [2]

Veopoz® is the first FDA-approved treatment for CHAPLE disease. Soliris® (eculizumab) has a similar mechanism of action as Veopoz® and has been used off label for the treatment of subjects with CHAPLE disease. Soliris® is approved for the treatment of other complement-mediated diseases such as paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome, generalized myasthenia gravis, and neuromyelitis optica spectrum disorder.

Guidelines

CHAPLE disease is an ultra-rare condition, and societal guidelines do not currently exist for treatment recommendations. Prior to the approval of

Veopoz®, management of patients with CHAPLE disease has primarily been supportive, including therapies such as:

- Corticosteroids, biologics, and immunomodulators to reduce intestinal inflammation.
- Intravenous or subcutaneous immunoglobulin therapy to treat hypogammaglobulinemia and prevent recurrent infections.
- Intravenous albumin to maintain oncotic pressure and reduce edema.
- Restricted diets excluding long chain fatty acids.
- Micronutrients to replace intestinal losses/malabsorption.
- Anti-coagulants and anti-platelet agents to treat and prevent the venous thromboses.
- Subcutaneous injections of octreotide to limit production & flow of chyle.
- Intestinal (small bowel) resections to remove the most leaky and inflamed sections of bowel or treat obstructions.
- Soliris® (eculizumab) used off-label.[3]

Criteria

Prior authorization is required.

Veopoz® is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of CD55-deficient protein-losing enteropathy (PLE) (CHAPLE disease); **AND**
2. Disease verified by genetic testing confirming biallelic CD55 loss-of-function mutation; **AND**
3. Member is 1 year of age or older; **AND**
4. Veopoz® will not be used concurrently with another complement inhibitor (e.g., Soliris® [eculizumab]); **AND**
5. Prescribed by, or in consultation with, a gastroenterologist or a physician specializing in rare genetic disorders; **AND**
6. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed (i **AND** ii):
        i. Single loading dose of 30 mg/kg (administered intravenously); **AND**
        ii. Maintenance dose of 10 mg/kg (maximum dose of 800 mg) once weekly (administered subcutaneously) starting on Day 8 and thereafter. If there is inadequate clinical response after at least 3 weekly doses (i.e., starting from week 4), may increase dose to 12 mg/kg (maximum dose of 800 mg); **OR**
    b. Regimen is supported by clinical practice guidelines. Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Veopoz® is considered medically necessary for continuation of therapy when **ALL** of the following are met:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Documentation of positive clinical response to therapy (e.g., improvement or stabilization of clinical symptoms [abdominal pain, diarrhea, and/or edema], increase in or stabilization of IgG concentrations, increase in growth percentile, reduction in hospitalizations, normalization of serum albumin levels); **AND**
3. Veopoz® will not be used concurrently with another complement inhibitor (e.g., Soliris® [eculizumab]); **AND**
4. Prescribed by, or in consultation with, a gastroenterologist or a physician specializing in rare genetic disorders; **AND**
5. Request meets one of the following (a, b, or c):
    a. Regimen prescribed does not exceed 10 mg/kg (maximum dose 800 mg) once weekly (administered subcutaneously); **OR**
    b. If documentation of inadequate clinical response after at least 3 weekly doses, then regimen prescribed does not exceed 12 mg/kg (maximum dose 800 mg) once weekly (administered subcutaneously); **OR**
    c. Regimen is supported by clinical practice guidelines. Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Approval Duration and Quantity Limits

	Initial Authorization	Subsequent Authorization(s)
Approval Duration	6 months	12 months
Quantity Limits	• Day 1: 30 mg/kg IV for 1 dose • Day 8 and thereafter: 10 mg/kg once weekly (may be increased to 12 mg/kg once weekly based on clinical response AFTER 3 weekly doses (i.e., starting from week 4) • Maximum weekly dose: 800 mg	• 10 mg/kg once weekly (may be increased to 12 mg/kg once weekly based on clinical response AFTER 3 weekly doses (i.e., starting from week 4) • Maximum weekly dose: 800 mg

Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

HCPCS	Description
J9376	Injection, pozelimab-bbfg, 1 mg

ICD-10	Description
D84.1	Defects in the complement system

NDC (and strength)	Labeler	Dosage	Pkg Size	Pkg Qty	Units/ Pkg
61755-0014-01 (400 mg/2 mL vial)	Regeneron Pharmaceuticals, Inc. (61755)	1 mg	1	EA	400

Compliance

1. Should conflict exist between the policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

[1] Veopoz® prescribing information (03/2024). Regeneron Pharmaceuticals, Inc.: Tarrytown, NY. Available online: www.veopoz.com. Accessed June 25, 2024.

[2] CDER Multi-Discipline Review of REGN3918 (pozelimab-bbfg) [FDA Application Review Files]. BLA 761339. Review completed August 18, 2023. Online: www.accessdata.fda.gov/drugsatfda_docs/nda/2023/761339Orig1s000TOC.cfm. Accessed August 28, 2024.

[3] CDER Multi-Discipline Review of REGN3918 (pozelimab-bbfg) [FDA Application Review Files]. BLA 761339. Review completed August 18, 2023. Online: www.accessdata.fda.gov/drugsatfda_docs/nda/2023/761339Orig1s000TOC.cfm. Accessed August 28, 2024.

Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources

may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

Criteria Change History

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		[#]
Signature			

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		[#]
Signature			

Change Date	Changed By	Description of Change	Version
10/18/2024	CAC	Criteria implementation. After initial review, move to April annual review to align with other enzyme therapy policies.	1
Signature William (Bill) Jagiello, DO			

CAC = Medicaid Clinical Advisory Committee