Keystone First VIP Choice

Medical Policy Bulletin

Title:
Pozelimab-bbfg (Veopoz™)
Policy #:
MA08.167

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.

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.

MEDICALLY NECESSARY

INITIAL THERAPY
Pozelimab-bbfg (Veopoz™) is considered medically necessary and, therefore, covered for the treatment of individuals one year of age and older with cluster of differentiation (CD)55-deficient protein-losing enteropathy (PLE), also known as CHAPLE (complement hyperactivation, angiopathic thrombosis and protein-losing enteropathy) disease, when **all** of the following are met:

- Presence of laboratory-confirmed genotype of biallelic CD55 loss-of-function mutation
- Presence of at least **one** of the following symptoms, attributable to CHAPLE disease, within the last six months (unless the individual is currently being treated with eculizumab [Soliris®] therapy with the willingness by the professional provider to discontinue the treatment before initiating treatment with pozelimab-bbfg [Veopoz]):
    - Hypoalbuminemia (serum albumin concentration of 3.2 g/dL or less)
    - Facial edema
    - Peripheral edema
    - Diarrhea
    - Abdominal pain
    - Thromboembolic event(s)
- Completion or update of meningococcal vaccination (in serogroups A, C, W and Y, and serogroup B) at least two weeks prior to the planned start of pozelimab-bbfg (Veopoz) therapy 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)

- Pozelimab-bbfg (Veopoz) is ordered by, or in consultation with, a professional provider who has the expertise to treat CHAPLE disease (e.g., Gastroenterology, Hematology, Immunology, rare genetic hematologic disease specialist)
- The individual will not be concurrently treated with any other complement inhibitors
- The individual does not have unresolved Neisseria meningitidis infection at the start of treatment with pozelimab-bbfg (Veopoz)

CONTINUATION THERAPY
Continuation of pozelimab-bbfg (Veopoz) will be considered to be medically necessary when all of the following are met:

- Hypoalbuminemia has improved or resolved from baseline levels
- Symptoms have improved or resolved from baseline levels

EXPERIMENTAL/INVESTIGATIONAL

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

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 service.

Guidelines

There is no Medicare coverage determination addressing pozelimab-bbfg (Veopoz), therefore, the Company policy is applicable.

Certain drugs are available only through the member's medical benefit (Part B benefit), depending on how the drug is prescribed, dispensed, or administered. For Medicare Advantage members, pozelimab-bbfg (Veopoz) is covered ONLY under a member's medical benefit (Part B benefit).

BENEFIT APPLICATION

Subject to the applicable Evidence of Coverage, pozelimab-bbfg (Veopoz) is covered under the medical benefits of the Company's Medicare Advantage products when the medical necessity criteria listed in this medical policy are met.

ADMINISTRATION GUIDELINES FROM THE PRODUCT'S PACKAGE INSERT

Day 1 (loading dose):
Administer a single 30 mg/kg dose by intravenous (IV) infusion after dilution

Day 8 and thereafter (maintenance dosage):
Inject 10 mg/kg as a subcutaneous (SC) 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
- All IV and SC doses must be prepared and administered by a healthcare provider

US FOOD AND DRUG ADMINISTRATION (FDA) STATUS

Pozelimab-bbfg (Veopoz) was approved by the FDA on August 18, 2023 for the treatment of individuals one year of age and older with CD55-deficient protein-losing enteropathy (PLE), also known as CHAPLE disease. Pozelimab-bbfg (Veopoz) is designated as an orphan drug by the FDA for this indication.

PEDIATRIC USE
The safety and effectiveness of pozelimab-bbfg (Veopoz) have not been established in pediatric individuals less than one year of age.

Description

Complement hyperactivation, angiopathic thrombosis and protein-losing enteropathy (PLE) or cluster of differentiation (CD)55-deficient PLE (CHAPLE disease) is an ultrarare disease (estimated at 100 individuals worldwide) caused by a recessive homozygous variant in the gene that encodes CD55, a complement regulating protein. The complement system is responsible for providing a defense for the individual by microbe destruction and immunity modulation. CD55 attaches to the surface of cells and prevents overactivation of the terminal complement system. Lack of CD55 results in intestinal inflammation and primary intestinal lymphangiectasia. The disease is characterized by hypoalbuminemia, hypogammaglobulinemia (resulting in susceptibility to recurrent bacterial infections such as Streptococcus pneumonia, Haemophilus influenzae, and Neisseria meningitidis), gastrointestinal symptoms (abdominal pain, nausea, vomiting, diarrhea), edema (facial and peripheral), and chronic malabsorption that results in micronutrient deficiencies (e.g., iron, ferritin, folate, calcium, magnesium, vitamin B12, vitamin D). Severe cases could result in the presence of pleural or pericardial effusions or abdominal ascites. Individuals experience anemia, growth retardation, recurrent respiratory infections, gastrointestinal obstruction and/or perforation, and severe thromboembolic vascular occlusions. The disease is often identified in infancy or early childhood due to the presence of clinical and laboratory evidence, but cases of the disease have also been identified in adults. Individuals with CHAPLE disease are treated with supportive care, including albumin and blood transfusions, dietary management (low fat, high protein, high medium-chain triglycerides), intravenous immunoglobulin (IVIG), immunosuppressive therapy, bowel resections, and supplementation of micronutrients and vitamins. There have been reports in the medical literature of individual case studies and small case series (Hagin et al. 2021; Hanna et al. 2019; Kaya 2023; Kurolap et al. 2017; Kurolap et al. 2019; Kurolap et al. 2023; Ohlsson et al. 2023; Ozen 2019; Ozen et al. 2021) in which individuals with CHAPLE disease were treated successfully with eculizumab (Soliris). The use is off-label as CHAPLE disease is not an FDA-approved use of the drug and there have not been any clinical trials reporting the efficacy and safety of the drug used for this indication. The normal course of the disease can result in early mortality due to thromboembolic events.

Pozelimab-bbfg (Veopoz) is a monoclonal immunoglobulin G4 (IgG4) antibody directed against the terminal complement protein C5 that inhibits terminal complement activation by blocking cleavage of C5 into C5a (anaphylatoxin) and C5b, thereby blocking the formation of the membrane-attack complex (C5b-C9, a structure mediating cell lysis).

The safety and efficacy of pozelimab-bbfg (Veopoz) were evaluated in a phase 2-phase 3, single-arm, multicenter, historically-controlled, open label clinical trial (NCT04209634). The primary outcome was the percentage of individuals who achieved normalization of serum albumin concentrations and improvement in their symptoms by week 24. Some secondary outcomes were number of individuals who had improvement in the signs and symptoms of the disease, percentage of individuals who maintained disease control, number of individuals with albumin infusions, time to normalization of serum albumin concentrations, absolute values of immunoglobulins (IgG, IgM, IgA) at week 24, time to normalization of total protein and percentage of individuals whose levels normalized, number of hospitalization days, quality of life measures, and safety measures. The treatment group consisted of ten individuals ranging in age from three to 19 years of age. The mean baseline serum albumin concentration for the individuals was 2.2 g/dL (range 1.1 to 2.9 g/dL). All ten of the individuals achieved normalization of their serum albumin and IgG concentrations by week 12 and maintained normal levels through at least 72 weeks of therapy. Seven of the participants underwent an abdominal computed tomography (CT) or magnetic resonance imaging (MRI) study both before and during treatment. All seven of the studies demonstrated resolution of mesenteric lymphadenopathy and small bowel wall thickening/enhancement. By week 36, all evaluable individuals had resolved the facial edema. By week 24, all evaluable individuals had resolved the peripheral edema. By week 48, the nine evaluable individuals increased their mean change from baseline in their weight-for-age and height-for-age percentiles by 15.5 and 11.2

respectively. Prior to the clinical trial, five of the ten involved individuals had received a total of 60 albumin transfusions in the previous year (48 weeks). In the year (48 weeks) after starting treatment with pozelimab-bbfg (Veopoz), only one individual required one albumin transfusion. Prior to the clinical trial, nine of the ten involved individuals has been hospitalized for a total of 268 days in the previous year (48 weeks). In the year (48 weeks) after starting treatment with pozelimab-bbfg (Veopoz), only two individuals were hospitalized for a total of seven days. Nine of the participants experienced a total of 47 treatment-emergent adverse events, but most were felt to be unrelated to the treatment. Treatment-related adverse events were considered to be mild, and no participant withdrew from the study or stopped treatment permanently.

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.

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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

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ICD - 10 Diagnosis Code Number(s)

D84.1 Defects in the complement system

K90.49 Malabsorption due to intolerance, not elsewhere classified

HCPCS Level II Code Number(s)

J9376 Injection, pozelimab-bbfg, 1 mg

Revenue Code Number(s)

N/A

Policy History

Revisions From MA08.167:

05/07/2024	The policy will become effective 05/07/2024. The following new policy has been developed to communicate the Company's coverage criteria for pozelimab-bbfg (Veopoz™).

Version Effective Date:
04/01/2024
Version Issued Date:
04/01/2024
Version Reissued Date:
N/A