Blue Cross Blue Shield Blue Care Network of Michigan

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Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

Effective Date: 04/11/2024

Zinplava™ (bezlotoxumab)

HCPCS: J0565

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved indication
   b. FDA approved age
   c. Prescribed by or in consultation with a gastroenterologist or infectious disease specialist
   d. Patient with a confirmed diagnosis of *Clostridioides difficile* infection (CDI) and stool test with toxin A/B positive results
   e. Patient at high risk for CDI recurrence e.g.
      i. Patients aged 65 years and older,
      ii. History of CDI in the past 6 months,
      iii. Immunocompromised state,
      iv. Severe CDI at presentation
      v. Clostridium difficile ribotype 027
   f. Used in conjunction with standard of care antibacterial agents (i.e. metronidazole or vancomycin)
   g. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list.

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limit: One infusion per lifetime
   b. Initial Authorization Period: 60 days
   c. Renewal Criteria: Not applicable as no further authorization will be provided. Safety and efficacy of repeat administration of Zinplava in patients with CDI has not been studied.

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Zinplava is a human monoclonal antibody that binds to Clostridium difficile toxin B, indicated to reduce recurrence of CDI in patients 18 years of age or older who are receiving antibacterial drug treatment of CDI and are at a high risk for CDI recurrence.

- CDI is one of the most common hospital-acquired (nosocomial) infections and is an increasingly frequent cause of morbidity and mortality among older adult hospitalized patients. Clostridium difficile colonizes the human intestinal tract after the normal gut flora has been altered by antibiotic therapy and is the causative organism of antibiotic-associated pseudomembranous colitis.

- Patients taking antibiotics are 7 to 10 times more likely to contract CDI. The overprescribing of antibiotics combined with poor hygiene and infection control on the part of healthcare workers make CDI a scourge in the nation's hospitals and nursing homes.

- Toxins A and B are the major virulence factors of Clostridium difficile. Toxins A and B mediate disease by disrupting the cytoskeletal structure of intestinal epithelial cells, resulting in inflammation and cell death. Toxin A ("enterotoxin") causes inflammation leading to mucosal injury and intestinal fluid secretion. Toxin B ("cytotoxin") is essential for the virulence of Clostridium difficile and is more potent than toxin A in mediating colonic mucosal damage. Ribotype 027 is a hypervirulent strain of Clostridium difficile found in 87% of patients who had a hypervirulent strain in the Zinplava study.

- The 2021 Infectious Diseases Society of America and Society for Healthcare Epidemiology of America (IDSA/SHEA) Guideline Update recommends use of adjunctive therapy for prophylaxis after one recurrent CDI episode treated with appropriate antibiotics.

    - These guidelines recommend the use of Zinplava for patients with recurrent CDI episode within the last 6 months, as an adjunctive treatment to antibiotics (fidaxomicin, vancomycin, etc.) rather than antibiotics alone. Zinplava is an IV administered monoclonal antibody that is given as a single infusion over 60 minutes.

    - The guidelines state the balance of benefits and harms favor adding Zinplava to standard of care antibiotics for patients with a CDI episode and at least 1 risk factor for recurrence (recurrent CDI episode within the last 6 months, age ≥ 65 years, immunocompromised host, and severe CDI on presentation), however treatment seems more favorable in patients with multiple risk factors of recurrent CDI and especially in patients with a prior CDI in the last 6 months. Current guidelines do not favor the use of Zinplava or fecal microbiota transplantation (FMT) over the other for prevention of recurrence of CDI. Zinplava was the only FDA approved option for prevention of recurrence of CDI when the 2021 IDSA/SHEA guidelines were published.

References:

1. Zinplava [prescribing information] Whitehouse Station, NJ; Merck Sharp and Dohme, Corp.; October 2016
2. Stuart Johnson, Valéry Lavergne, Andrew M Skinner, Anne J Gonzales-Luna, Kevin W Garey, Ciaran P Kelly, Mark H Wilcox, Clinical Practice Guideline by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA): 2021 Focused Update Guidelines on Management of *Clostridioides difficile* Infection in Adults, *Clinical Infectious Diseases*, Volume 73, Issue 5, 1 September 2021, Pages e1029–e1044, https://doi.org/10.1093/cid/ciab549
3. Bezlotoxumab (BEZ) Alone and With Actoxumab (ACT) for Prevention of Recurrent C. difficile Infection (rCDI) in Patients on Standard of Care (SoC) Antibiotics: Integrated Results of 2 Phase 3 Studies (MODIFY I and MODIFY II) Open Forum Infect Disease, Fall 2015, Vol 2, issue suppl 1.
4. Wilcox MH, Gerding D, Poxton I, et al. Bezlotoxumab alone and with actoxumab for prevention of recurrent C. difficile infection in patients on standard of care antibiotics: Integrated results of two Phase III studies (MODIFY I and MODIFY II) [oral presentation]. ID Week; San Diego, CA; October 7-11, 2015
5. Guidelines for Diagnosis, Treatment, and Prevention of Clostridium difficile Infections. The American Journal of Gastroenterology, Volume 108, April 2013.
6. Kelly C, Fischer M, Allegretti J, et al. ACG Clinical Guidelines: Prevention, Diagnosis, and Treatment of Clostridioides difficile Infections. The American Journal of Gastroenterology: June 2021 - Volume 116 - Issue 6 - p 1124-1147.

<table>
<tr><th colspan="3">Policy History</th></tr>
<tr><th>#</th><th>Date</th><th>Change Description</th></tr>
<tr><td>1.9</td><td>Effective Date: 04/11/2024</td><td>Annual review of criteria was performed, no changes were made</td></tr>
<tr><td>1.8</td><td>Effective Date: 04/06/2023</td><td>Updated the approval duration to allow for 60 day requirement</td></tr>
<tr><td>1.7</td><td>Effective Date: 04/14/2022</td><td>Annual review of criteria was performed, no changes were made.</td></tr>
<tr><td>1.6</td><td>Effective Date: 04/08/2021</td><td>Annual review of criteria was performed, no changes were made.</td></tr>
<tr><td>1.5</td><td>Effective Date: 4/16/2020</td><td>Annual review of criteria was performed, no changes were made.</td></tr>
<tr><td>1.4</td><td>Effective Date: 10/01/2019</td><td>UM medical management system update for BCNA and MAPPO
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table></td></tr>
<tr><td>1.3</td><td>Effective Date: 05/09/2019</td><td>Annual review of criteria was performed, no changes were made.</td></tr>
<tr><td>1.2</td><td>Effective Date: 07/01/2017</td><td>UM medical management system update for BCBS and BCN
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>No</td></tr><tr><td>BCNA</td><td>No</td></tr></table></td></tr>
<tr><td>1.1</td><td>Effective Date: 05/03/2018</td><td>Annual review of criteria was performed, no changes were made.</td></tr>
<tr><td>1.0</td><td>Effective Date: 05/04/2017</td><td>New Drug Review
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>No</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>No</td></tr><tr><td>BCNA</td><td>No</td></tr></table></td></tr>
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** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*