



Nonprofit corporations and independent licensees
of the Blue Cross and Blue Shield Association

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.

P&T Date: 04/10/2025

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, fidaxomicin, or vancomycin)
 - g. Not to be used in combination with fecal microbiota products, such as Rebyota® or Vowst™
 - h. 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.

This policy and any information contained herein is the property of Blue Cross Blue Shield of Michigan and its subsidiaries, is strictly confidential, and its use is intended for the P&T committee, its members and BCBSM employees for the purpose of coverage determinations.

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 \geq 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.
- In Zinplava's Phase III trial, standard of care antibiotics used were metronidazole (48%), vancomycin (48%), and fidaxomicin (4%).

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>

This policy and any information contained herein is the property of Blue Cross Blue Shield of Michigan and its subsidiaries, is strictly confidential, and its use is intended for the P&T committee, its members and BCBSM employees for the purpose of coverage determinations.

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.

Policy History												
#	Date	Change Description										
2.0	Effective Date: 05/27/2025 P&T Date: 04/10/2025	Updated criteria to include: Not to be used in combination with fecal microbiota products, such as Rebyota or Vowst										
1.9	Effective Date: 04/11/2024	Annual review of criteria was performed, no changes were made										
1.8	Effective Date: 04/06/2023	Updated the approval duration to allow for 60 day requirement										
1.7	Effective Date: 04/14/2022	Annual review of criteria was performed, no changes were made.										
1.6	Effective Date: 04/08/2021	Annual review of criteria was performed, no changes were made.										
1.5	Effective Date: 04/16/2020	Annual review of criteria was performed, no changes were made.										
1.4	Effective Date: 10/01/2019	UM medical management system update for BCNA and MAPPO <table border="1" style="margin-left: auto; margin-right: auto;"> <thead> <tr> <th>Line of Business</th> <th>PA Required in Medical Management System (Yes/No)</th> </tr> </thead> <tbody> <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> </tbody> </table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	Yes	BCN	Yes	MAPPO	Yes	BCNA	Yes
Line of Business	PA Required in Medical Management System (Yes/No)											
BCBS	Yes											
BCN	Yes											
MAPPO	Yes											
BCNA	Yes											
1.3	Effective Date: 05/09/2019	Annual review of criteria was performed, no changes were made.										
1.2	Effective Date: 05/03/2018	Annual review of criteria was performed, no changes were made.										
1.1	Effective Date: 07/01/2017	UM medical management system update for BCBS and BCN <table border="1" style="margin-left: auto; margin-right: auto;"> <thead> <tr> <th>Line of Business</th> <th>PA Required in Medical Management System (Yes/No)</th> </tr> </thead> <tbody> <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> </tbody> </table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	Yes	BCN	Yes	MAPPO	No	BCNA	No
Line of Business	PA Required in Medical Management System (Yes/No)											
BCBS	Yes											
BCN	Yes											
MAPPO	No											
BCNA	No											

This policy and any information contained herein is the property of Blue Cross Blue Shield of Michigan and its subsidiaries, is strictly confidential, and its use is intended for the P&T committee, its members and BCBSM employees for the purpose of coverage determinations.

1.0	Effective Date: 05/04/2017	<p data-bbox="464 136 659 170">New Drug Review</p> <table border="1" data-bbox="483 201 1367 411"> <thead> <tr> <th data-bbox="483 201 964 268">Line of Business</th> <th data-bbox="964 201 1367 268">PA Required in Medical Management System (Yes/No)</th> </tr> </thead> <tbody> <tr> <td data-bbox="483 268 964 302">BCBS</td> <td data-bbox="964 268 1367 302">No</td> </tr> <tr> <td data-bbox="483 302 964 336">BCN</td> <td data-bbox="964 302 1367 336">Yes</td> </tr> <tr> <td data-bbox="483 336 964 369">MAPPO</td> <td data-bbox="964 336 1367 369">No</td> </tr> <tr> <td data-bbox="483 369 964 411">BCNA</td> <td data-bbox="964 369 1367 411">No</td> </tr> </tbody> </table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	No	BCN	Yes	MAPPO	No	BCNA	No
Line of Business	PA Required in Medical Management System (Yes/No)											
BCBS	No											
BCN	Yes											
MAPPO	No											
BCNA	No											

** 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>.*