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.

P&T Date: 02/13/2025

Rebyota® (fecal microbiota, live-jslm)

HCPCS: J1440

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. Had at least 1 recurrence after a primary episode of *Clostridioides difficile* infection (CDI) and completion of one or more round(s) of standard-of-care antibiotic therapy (ex: metronidazole, vancomycin, fidaxomicin) OR two or more episodes of severe CDI resulting in hospitalization within the past year
   d. A *C. difficile* stool test with toxin A/B positive results within the previous 30 days
   e. Not to be used in combination with Zinplava™ or Vowst™
   f. 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 Limits: Aligns with FDA recommended dosing
   b. Authorization Period: 60 days
   c. Renewal Criteria: Not applicable as no further authorization will be provided.

***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:

- Rebyota is indicated for the prevention of recurrence of CDI in individuals 18 years of age and older following antibiotic treatment for recurrent CDI.

- In the pivotal Phase III PUNCH CD3 trial, which was utilized for FDA approval of this therapy, inclusion criteria included documentation of recurrent CDI (defined as one or more recurrences after a primary episode) in participants who had completed one or more rounds of standard-of-care antibiotic therapy OR had two or more episodes of severe CDI resulting in hospitalization in the last year, a positive stool test within 30 days of enrollment, and participants must have been taking or have just been prescribed antibiotics to control recurrent CDI symptoms. There was a 24-72 hour antibiotic washout period prior to Rebyota therapy. These specific inclusion criteria are included in the policy due to the narrow treatment window that Rebyota offers.

    - Patients were treated with a single 150 mL rectal dose. The primary endpoint was treatment success, defined as the absence of CDI diarrhea within 8 weeks of study treatment. The estimated rate of treatment success was 70.6% in the Rebyota group (95% Credible Interval, 64.1%-76.8%) compared to placebo 57.5% (95% Credible Interval, 48.1%-67.1%). In this trial, patients who did not experience treatment success at week 8 were given a 2nd dose. Determining treatment failure can take up to 8 weeks, and an authorization period of 2 months would allow for a one-time repeat dose of Rebyota after the initial authorization period. Data that supports continued Rebyota treatment does not exist. Currently, data only supports one repeat course of treatment.

- The 2021 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 Rebyota alternative, 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. Zinplava is FDA approved to reduce the 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.

    - The guidelines state the balance of benefits and harms favor adding Zinplava to SOC 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 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. Rebyota [Package Insert]. Parsippany, NJ. Ferring Pharmaceuticals Inc. November, 2022.
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. Khanna, Sahil et al. "Efficacy and Safety of RBX2660 in PUNCH CD3, a Phase III, Randomized, Double-Blind, Placebo-Controlled Trial with a Bayesian Primary Analysis for the Prevention of Recurrent Clostridioides difficile Infection." Drugs vol. 82,15 (2022): 1527-1538. doi:10.1007/s40265-022-01797-x
4. ClinicalTrials.gov. Microbiota Restoration Therapy for Recurrent Clostridium Difficile Infection (PUNCHCD2). Available at: https://clinicaltrials.gov/ct2/show/results/NCT02299570

<table>
<tr><th colspan="3">Policy History</th></tr>
<tr><th>#</th><th>Date</th><th>Change Description</th></tr>
<tr><td>1.4</td><td>Effective Date: 03/31/2025

P&T Date: 02/13/2025</td><td>Updated criteria to include not to be used in combination with Zinplava or Vowst.</td></tr>
<tr><td>1.3</td><td>Effective Date: 02/08/2024</td><td>Annual review – no changes to the criteria were made.</td></tr>
<tr><td>1.2</td><td>Effective Date: 03/01/2023</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>1.1</td><td>Effective Date: 02/02/2023</td><td>New policy</td></tr>
<tr><td>1.0</td><td>Effective Date: 01/05/2023</td><td>UM medical management system update for BCBSM 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>
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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.*