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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.

Effective Date: 02/08/2024

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
 - 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

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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 \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 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>

Policy History												
#	Date	Change Description										
1.3	Effective Date: 02/08/2024	Annual review – no changes to the criteria were made.										
1.2	Effective Date: 03/01/2023	UM medical management system update for BCNA and MAPPO <table border="1" data-bbox="483 373 1365 583"> <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
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BCBS	Yes											
BCN	Yes											
MAPPO	Yes											
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1.1	Effective Date: 02/02/2023	New policy										
1.0	Effective Date: 01/05/2023	UM medical management system update for BCBSM and BCN <table border="1" data-bbox="483 730 1365 940"> <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
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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>.

**Blue Cross Blue Shield/Blue Care Network of Michigan
Medication Authorization Request Form
Rebyota® (fecal microbiota, live-jslm) HCPCS CODE: J1440**



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This form is to be used by participating physicians to obtain coverage for Zinplava. For commercial members only, please complete this form and submit via fax to 1-877-325-5979. If you have any questions regarding this process, please contact BCBSM Provider Relations and Servicing or the Medical Drug Helpdesk at 1-800-437-3803 for assistance.

PATIENT INFORMATION	PHYSICIAN INFORMATION
Name	Name
ID Number	Specialty
D.O.B. <input type="checkbox"/> Male <input type="checkbox"/> Female	Address
Pt weight (in kg) Date recorded: _____	City /State/Zip
Diagnosis	Phone/Fax: P: () - F: () -
Drug Name	NPI
Dose and Quantity	Contact Person
Directions	Contact Person Phone / Ext.
Date of Service(s)	

STEP 1: DISEASE STATE INFORMATION

1. Initiation or Continuation of therapy? Initiation Continuation *Date patient started therapy:* _____

2. Please specify the location of administration (e.g. name of facility):

3. Please provide the NPI number for the place of administration: _____

4. Initiation of therapy:

- a. Please check the patient's diagnosis:
 - Prevention of repeated Clostridium Difficile Infection (CDI) with recurrent active infection
 - Other: _____
- b. Did the patient have at least one 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)?
 - No Yes
- c. Did the patient have two more episodes of severe CDI resulting in hospitalization within the past year?
 - No Yes, dates of hospitalization: _____
- d. Does the patient have a positive *C. difficile* stool test with toxin A/B within the past 30 days?
 - No Yes, date of test: _____
- e. Will this patient be receiving Rebyota with Zinplava? Yes No

5. Please add any other supporting medical information necessary for our review

Coverage will not be provided if the prescribing physician's signature and date are not reflected on this document.

Request for expedited review: I certify that applying the standard review time frame may seriously jeopardize the life or health of the member or the member's ability to regain maximum function

Physician's Name	Physician Signature	Date
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Step 2: Checklist	<input type="checkbox"/> Form Completely Filled Out <input type="checkbox"/> Attached Chart Notes	<input type="checkbox"/> Weight (specify lb or kg) , BSA
Step 3: Submit	By Fax: BCBSM Specialty Pharmacy Mailbox 1-877-325-5979	By Mail: BCBSM Specialty Pharmacy Program P.O. Box 312320, Detroit, MI 48231-2320

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