

## Clinical Policy: Fecal Microbiota, Live-jslm (Rebyota)

Reference Number: PA.CP.PHAR.613

Effective Date: 08/2023

Last Review Date: 01/2026

### Description

Fecal microbiota, live-jslm (Rebyota™) is a fecal microbiota suspension manufactured from human fecal matter sourced from qualified donors.

### FDA Approved Indication(s)

Rebyota is indicated for the prevention of recurrence of *Clostridioides difficile* infection (CDI) in individuals 18 years of age and older, following antibiotic treatment for recurrent CDI.

Limitation(s) of use: Rebyota is not indicated for treatment of CDI.

### Policy/Criteria

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of PA Health & Wellness® that Rebyota is **medically necessary** when the following criteria are met:

#### I. Initial Approval Criteria

##### A. Prevention of *Clostridioides difficile* Infection (must meet all):

1. Diagnosis of CDI confirmed by documentation of positive *Clostridioides difficile* test;
2. Age  $\geq$  18 years;
3. Member has recurrent CDI as evidenced by one of the following (a or b):
  - a. At least 2 episodes of CDI recurrence after a primary episode (i.e., total 3 episodes);
  - b. At least 2 episodes of severe CDI resulting in hospitalization within the last year;
4. Member has received at least 10 consecutive days of antibiotic therapy for the current CDI (e.g., vancomycin, fidaxomicin);
5. The current CDI is controlled (< 3 unformed/loose stools/day for 2 consecutive days [i.e., diarrhea, or Bristol Stool Scale type 6-7]);
6. Member has not previously received Rebyota, Vowst™, or prior fecal microbiota transplant;
7. Dose does not exceed a single dose of 150 mL.

**Approval duration: 3 months (1 dose only)**

##### B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

#### II. Continued Therapy

##### A. Prevention of *Clostridioides difficile* Infection (must meet all):

1. Re-authorization is not permitted as the efficacy of repeat courses of Rebyota has not been sufficiently established (*see Appendix D*).

**Approval duration: Not applicable**

**B. Other diagnoses/indications (must meet 1 or 2):**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.

**Approval duration: Duration of request or 12 months (whichever is less); or**

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

**III. Diagnoses/Indications for which coverage is NOT authorized:**

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

CDI: *Clostridioides difficile* infection

FDA: Food and Drug Administration

IDSA: Infectious Diseases Society of America

*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.*

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Dificid <sup>®</sup> (fidaxomicin)	200 mg PO BID for 10 days; for recurrences, may use alternative regimen of 200 mg PO BID for 5 days, followed by QOD for 20 days	See regimen
vancomycin	125 mg PO QID for 10 days; for recurrences, may use a tapered and pulsed regimen	See regimen

*Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) when the drug is available by both brand and generic.*

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s): severe allergic reactions (e.g., anaphylaxis) to any component of Rebyota
- Boxed warning(s): none reported

*Appendix D: General Information*

- Both the Infectious Diseases Society of America (IDSA) and the American College of Gastroenterology recommend fecal microbiota transplantation for patients experiencing their second or further recurrence of CDI.

- Approximately 35% of CDI patients experience recurrence after the initial treatment and resolution of diarrhea. Of those who have a primary recurrence, 40% will have another CDI episode, and after 2 recurrences, the chance of an additional episode increases to as high as 65%.
- Per the 2017 IDSA Clinical Practice Guidelines for CDI:
  - An incident case is one with a new primary symptom onset (i.e., in the previous 8 weeks, there was not an episode of positive symptoms with positive *Clostridioides difficile* result) and positive *Clostridioides difficile* assay result.
  - A recurrent infection is an episode of symptom onset with a positive assay result following an episode with positive assay result in the previous 2-8 weeks.
- Per the 2021 IDSA Focused Update for CDI in Adults:
  - Fidaxomicin is the preferred first-line treatment for patients with recurrent CDI episodes.
  - Vancomycin (in a tapered and pulsed regimen or as a standard course) is an alternative treatment for CDI recurrence.
  - Bezlotoxumab (Zinplava<sup>®</sup>) is an adjunctive treatment that may be used in addition to standard of care antibiotics for patients with a recurrent CDI episode within the last 6 months.
  - Prior to fecal microbiota transplantation, appropriate antibiotic treatments for at least 2 recurrences (i.e., 3 CDI episodes) should be tried.
  - Examples of treatment regimens for recurrence:
    - Vancomycin 125 mg PO QID for 10 days (may be followed by rifaximin 400 mg PO TID for 20 days)
    - Tapered and pulsed regimens of vancomycin (e.g., vancomycin PO 125 mg QID for 10 to 14 days, then BID for 1 week, then QD for 1 week, then every 2 or 3 days for 2 to 8 weeks)
    - Fidaxomicin 200 mg PO BID for 10 days
    - Fidaxomicin 200 mg PO BID for 5 days followed by once every other day for 20 days
    - Fecal microbiota transplantation
    - Bezlotoxumab 10 mg/kg IV once during administration of standard of care antibiotics
- The Bristol Stool Scale is a tool to define stool types. Types 1-2 indicate constipated stool. Types 6-7 indicate diarrheal stool.
  - Type 1: separate hard lumps, like nuts
  - Type 2: sausage-shaped but lumpy
  - Type 3: like a sausage but with cracks on its surface
  - Type 4: like a sausage or snake, smooth and soft
  - Type 5: soft blobs with clear-cut edges (passed easily)
  - Type 6: fluffy pieces with ragged edges, a mushy stool
  - Type 7: watery, no solid pieces (entirely liquid)
- Repeat courses: In the event of treatment failure (i.e., CDI diarrhea) within the first 8 weeks of blinded treatment, participants in the PUNCH CD3 phase 3 study were allowed to receive an open-label second treatment course of Rebyota. However, only 41/180 (22.8%) patients who received an initial course of Rebyota received this second course, and of those 41, only 22 (53.8% of the patients who received a second treatment course;

12.2% of the original population) ultimately achieved treatment success. Given that this was an open-label treatment and included a relatively small sample, this is considered insufficient data to support a second treatment course at this time. In addition, the FDA label indicates only 1 dose should be administered and does not address repeat courses.

**V. Dosage and Administration**

Indication	Dosing Regimen	Maximum Dose
Prevention of CDI	Administer a single dose of 150 mL rectally of Rebyota 24 to 72 hours after the last dose of antibiotics for CDI	See regimen

**VI. Product Availability**

Suspension (a single dose is 150 mL)

**VII. References**

1. Rebyota Prescribing Information. Parsippany, NJ: Ferring Pharmaceuticals Inc; November 2022. Available at: [www.rebyota.com](http://www.rebyota.com). Accessed October 23, 2025.
2. Khanna S, Assi M, Lee C, Yoho D, 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*. 2022; 82(15): 1527-1538.
3. Rebiotix Inc. Microbiota restoration therapy for recurrent *Clostridium difficile* infection (PUNCHCD3). *ClinicalTrials.gov*. Available at: <https://clinicaltrials.gov/ct2/show/NCT03244644>. Accessed October 31, 2023.
4. Rebiotix Inc. Microbiota restoration therapy for recurrent *Clostridium difficile* infection (PUNCHCD2). *ClinicalTrials.gov*. Available at: <https://clinicaltrials.gov/ct2/show/NCT02299570>. Accessed October 31, 2023.
5. Lessa FC, Mu Y, Bamber WM et al. Burden of *Clostridium difficile* infection in the United States. *N Engl J Med*. 2015 Feb 26;372(9):825-34. doi: 10.1056/NEJMoa1408913
6. McDonald LC, Gerding DN, Johnson S, et al. Clinical practice guidelines for *Clostridium difficile* infection in adults and children: 2017 updated by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). *Clin Infect Dis*. March 2018;66(7):987-994.
7. Johnson S, Lavergne V, Skinner AM, et al. 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. *CID* 2021; 73 (1 September): e1029-1044.
8. Kelly CR, Fischer M, Allegretti JR, et al. ACG clinical guidelines: Prevention, diagnosis, and treatment of *Clostridioides difficile* infections. *Am J Gastroenterol*. 2021; 116: 1124 - 1147.
9. Caroff DA, Edelstein PH, Hamilton K, et al. The Bristol stool scale and its relationship to *Clostridium difficile* infection. *J Clin Microbiol*. 2014; 52(9): 3437-3439.
10. Dubberke ER, Lee CH, Orenstein R, et al. Results From a Randomized, Placebo-Controlled Clinical Trial of a RBX2660-A Microbiota-Based Drug for the Prevention of Recurrent *Clostridium difficile* Infection. *Clin Infect Dis*. 2018 Sep 28;67(8):1198-1204.
11. Peery AF, Kelly CR, Kao D, et al. AGA Clinical Practice Guideline on Fecal Microbiota-Based Therapies for Select Gastrointestinal Diseases. *Gastroenterology*. 2024 Mar; 166(3): 409-434.

**Coding Implications**

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J1440	Fecal microbiota, live - jslm, 1 ml

Reviews, Revisions, and Approvals	Date
Policy created	07/2023
1Q 2024 annual review: no significant changes; references reviewed and updated.	01/2024
1Q 2025 annual review: no significant changes; references reviewed and updated.	01/2025
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