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

Reference Number: PA.CP.PHAR.613
Effective Date: 08/2023
Last Review Date: 07/2023

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 ≥ 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*).

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.LTSS.PHAR.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 for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Dificid® (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® (generic) when the drug is available by brand name only and generic (Brand name®) 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®) 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. Accessed December 12, 2022.
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 December 14, 2022.
4. Rebiotix Inc. Microbiota restoration therapy for recurrent Clostridium difficile infection (PUNCHCD2). ClinicalTrials.gov. Available at: https://clinicaltrials.gov/ct2/show/NCT02299570. Accessed December 14, 2022.
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.

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	P&T Approval Date
Policy created	07/2023	