Original Effective Date: 05/31/2023
Current Effective Date: 01/31/2024
Last P&T Approval/Version: 01/31/2024
Next Review Due By: 01/2025
Policy Number: C25213-A

Rebyota (fecal microbiota, live-jslm)

PRODUCTS AFFECTED

Rebyota (fecal microbiota, live-jslm)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Prevention of recurrence of Clostridioides difficile infection (CDI)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. PREVENTION OF RECURRENCE OF CDI:
   1. Documentation member has a positive stool test within the last 30 days for Clostridioides difficile with the capability to produce toxins (e.g., polymerase chain reaction, or enzyme immunoassay)
      AND

2. Prescriber attestation that member has experienced at least 2 recurrent Clostridioides difficile infections (CDI) (i.e., 3 or more CDI episodes)
   AND
3. Documentation member has completed a full course of antibiotic therapy (e.g., oral vancomycin or fidaxomicin) for the most recent CDI episode. [DOCUMENTATION REQUIRED]
   AND
4. The member's current CDI episode must be controlled (i.e., reduced stool frequency)
   AND
5. Prescriber attests member will receive Rebyota within 24 to 72 hours of completion of the antibiotic course
   AND
6. Documentation FMT (fecal microbiota transplant) has been tried and failed or is unavailable from a reputable source (per guideline recommendation)
   AND
7. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Rebyota (fecal microbiota, live-jslm) include: Severe allergic reactions (e.g., anaphylaxis) to any component of Rebyota]

CONTINUATION OF THERAPY:
NA

DURATION OF APPROVAL:
Initial authorization: 1 (150ml) treatment, Continuation of Therapy: NA

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a board-certified infectious disease specialist or gastroenterologist [If prescribed in consultation, consultation notes must be submitted with initial request]

AGE RESTRICTIONS:

18 years of age and older

QUANTITY:
1 (150ml) treatment

PLACE OF ADMINISTRATION:
The recommendation is that rectal medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-hospital facility-based location.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Rectal administration

DRUG CLASS:
Live Fecal Microbiota (Human)

FDA-APPROVED USES:
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 of Use: Rebyota is not indicated for treatment of CDI.

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:

Warnings and Precautions
Because Rebyota (fecal microbiota, live-jslm) is manufactured from human fecal matter it may carry a risk of transmitting infectious agents. Any infection suspected by a physician possibly to have been transmitted by this product should be reported by the physician or other healthcare provider to Ferring Pharmaceuticals, Inc.
Appropriate medical treatment must be immediately available in the event an acute anaphylactic reaction occurs following administration of Rebyota (fecal microbiota, live-jslm).
Rebyota (fecal microbiota, live-jslm) is manufactured from human fecal matter and may contain food allergens. The potential for Rebyota to cause adverse reactions due to food allergens is unknown.

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
IDSA and SHEA clinical practice guidelines on management of Clostridioides difficile infection in adults (Clin Infect Dis. 2021)
II. In Patients With Recurrent CDI Episode(s), Should Fidaxomicin Be Used Rather Than Vancomycin? Recommendation: I. In patients with recurrent CDI episodes, we suggest fidaxomicin (standard or extended-pulsed regimen) rather than a standard course of vancomycin (conditional recommendation, low certainty evidence). Comment: Vancomycin in a tapered and pulsed regimen or vancomycin as a standard course are acceptable alternatives for a first CDI recurrence. For patients with multiple recurrences, vancomycin in a tapered and pulsed regimen, vancomycin followed by rifaximin, and fecal microbiota transplantation are options in addition to fidaxomicin.

ACG Clinical Guidelines: Prevention, diagnosis, and treatment of Clostridioides difficile infections (Am J Gastroenterol, 2021)
FMT for recurrent CDI Recommendations
14. We recommend patients experiencing their second or further recurrence of CDI be treated with FMT to prevent further recurrences (strong recommendation, moderate quality of evidence).
15. We recommend FMT be delivered through colonoscopy (strong recommendation, moderate quality of evidence) or capsules (strong recommendation, moderate quality of evidence) for treatment of rCDI; we suggest delivery by enema if other methods are unavailable (conditional recommendation, low quality of evidence).
16. We suggest repeat FMT for patients experiencing a recurrence of CDI within 8 weeks of an initial FMT (conditional recommendation, very low quality of evidence)

Rebyota (fecal microbiota, live-jslm) is a fecal microbiota suspension for rectal administration. It is manufactured from human fecal matter sourced from qualified donors and processed into 150mL dose containing between $1x10^8$ and $5x10^{10}$colony forming units (CFU) per mL of fecal microbes including > $1x10^5$ CFU/mL of Bacteroides.
The mechanism of action of Rebyota (fecal microbiota, live-jslm) has not been established, however it is a proprietary consortium of diverse spore-forming and non- spore-forming bacteria, which is thought to restore the gastrointestinal flora.
Rebyota (fecal microbiota, live-jslm) 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. Fecal microbiota, live-jslm is available as Rebyota in 150mL suspension for rectal administration which includes an administration set.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Rebyota (fecal microbiota, live-jslm) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Rebyota (fecal microbiota, live-jslm) include: severe allergic reactions (e.g., anaphylaxis) to any component of Rebyota.

OTHER SPECIAL CONSIDERATIONS:
Patient should empty their bladder and bowel, if possible, prior to the enema. No additional bowel preparation is required.
• A single dose of Rebyota is 150 mL.
• Administer Rebyota 24 to 72 hours after the last dose of antibiotics for CDI.
• Antibiotics should be avoided for 8 weeks following administration.
Food allergens: Rebyota may contain food allergens. The potential for adverse reactions due to food allergens is unknown.

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
J1440	Fecal microbiota, live - jslm, 1 mL

AVAILABLE DOSAGE FORMS:
Rebyota SUSP 150ML

REFERENCES

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4. Johnson, S., Lavergne, V., Skinner, A. M., Gonzales-Luna, A. J., Garey, K. W., Kelly, C. P., & Wilcox, M. H. (2021). 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, 73(5). https://doi.org/10.1093/cid/ciab549
5. Dubberke ER, 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;67(8):1198–1204. doi:10.1093/cid/ciy259
6. Gupta S, et al. Fecal microbiota transplantation: in perspective. Therap Adv Gastroenterol.

2016;9(2):229–239. doi:10.1177/1756283X15607414
7. Langdon A, et al. Microbiota restoration reduces antibiotic-resistant bacteria gut colonization in patients with recurrent Clostridioides difficile infection from the open-label PUNCH CD study. Genome Med. 2021;13(1):28. doi:10.1186/s13073-021-00843-9
8. Enforcement policy regarding investigational new drug requirements for use of Fecal Microbiota for Transplantation to Treat Clostridioides difficile Infection Not Responsive to Standard Therapies Guidance for Industry U.S. Department of Health and Human Services Food and Drug Administration Center for Biologics Evaluation and Research November 2022 Retrieved February 9, 2023, from https://www.fda.gov/media/86440/download

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Prescriber Requirements Coding/Billing Information Available Dosage Forms References	Q1 2024
NEW CRITERIA CREATION	Q2 2023