These Clinical Guidelines have been created using resources that were current as of the "Reviewed" date noted at the beginning of the document. Clinicians should refer to the manufacturer's Prescribing Information (or equivalent) for the most up-to-date information. While CarepathRx has published these Clinical Guidelines after a close review of available literature and a clinical review process, given the evolving nature and complexity of modern pharmaceutical products, CarepathRx does not and cannot warrant or guarantee that these Clinical Guidelines reflect the objectively best or highest standard of care at any given time.

Nothing within these Clinical Guidelines is intended to supersede or interfere with any individual clinician's decision-making or professional judgment with respect to either (1) prescribing or dispensing the drug or product in question or (2) the overall treatment plan for an individual patient.

Fecal microbiota, live (Rebyota) Clinical Guideline for Home Administration

Section: Clinical Guideline
Compliance: ACHC Infusion Pharmacy
ACHC Standards: N/A
URAC Standards: N/A
Policy ID: CG013
Effective: 9/3/2024
Reviewed: N/A
Revised: N/A
Approved by, Title and Date Approved: Kathleen Patrick, President, 9/3/24

I. BACKGROUND

Fecal microbiota, live (Rebyota) is a rectally administered suspension indicated for the treatment of recurrent *Clostridioides difficile* (C. Diff.) infection in patients 18 years or older. Fecal microbiota, live is manufactured from human fecal matter sourced from qualified donors. The human fecal matter is tested for a panel of transmissible pathogens. Donors do not have dietary restrictions with respect to potential food allergens. The fecal microbiota suspension is the filtrate generated by processing the fecal matter in a pre-defined ratio with a solution of polyethylene glycol (PEG) 3350 and saline. Each 150mL dose contains between $1x10^8$ and $5x10^{10}$ colony forming units (CFU) per mL of fecal microbes including $>1x10^5$ CFU/mL of *Bacteroides*. The suspension should be administered 24-72 hours after last antibiotic dose for C. Diff infection. The following outlines the procedures for servicing patients in need of outpatient fecal microbiota, live suspension administered rectally.

II. PATIENT ACCEPTANCE CRITERIA

A. All candidates for home care service must be evaluated by the clinician(s) and deemed appropriate to receive home care based upon the dispensing pharmacy's admission criteria.

B. The decision to administer a first dose in the home by a field nurse will be determined on a case-by-case basis and reviewed by nursing and pharmacy management. The following criteria will be evaluated:

1. Prescriber preference
2. Allergy profile (including food allergies)
3. Age
4. Other relevant social and/or medical history

C. Physician orders for fecal microbiota, live must include:

1. Drug
2. Dose
3. Route of administration
4. Frequency of administration
5. Emergency medications per protocol
6. Routine lab monitoring, if applicable

D. Baseline labs or tests prior to starting therapy

E. Dispensing pharmacy treatment epinephrine protocol for anaphylaxis will be instituted unless more comprehensive patient-specific orders are provided by physician. See Appendix A (Nursing CarepathRx policy on *Management of Allergic/Anaphylactic Reactions*)

III. PHARMACOLOGY OVERVIEW

Refer to manufacturer's full Prescribing Information for most up to date information

A. Indications: Prevention of recurrent C. Diff infection in individuals 18 years of age and older following antibiotic treatment for recurrent C. Diff.

B. Dosing: For rectal administration only. Fecal microbiota, live is a one-time dose provided as a 150 mL suspension administered rectally 24-72 hours after last antibiotic dose.

C. Dose Adjustment: no dose adjustments

D. Duration: One-time single dose

E. Contraindications: Severe anaphylaxis reactions such as anaphylaxis to any component of fecal microbiota, live.

F. Warnings and Precautions:

1. Transmissible infectious agents: Because fecal microbiota, live 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.

2. Management of acute allergic reactions: Appropriate medical treatment must be immediately available in the event of an acute anaphylactic reaction following administration.

3. Potential presence of food allergens: Fecal microbiota, live is manufactured from human fecal matter and may contain food allergens. The potential for fecal microbiota, live to cause adverse reactions due to food allergens is unknown.

4. Pregnancy and lactation: Fecal microbiota, live is not absorbed systemically following rectal administration and maternal use is not expected to result in fetal exposure. Breastfeeding is not expected to result in exposure of the child to fecal microbiota, live.

G. Pharmacokinetics: Fecal microbiota, live is not systemically absorbed.

H. Adverse Reactions: Abdominal pain (8.9%), diarrhea (7.2%), Abdominal distention (3.9%), flatulence (3.3%), and nausea (3.3%).

I. Drug Interactions: drug-drug interactions may exist. Consult interaction database for patient specific assessment.

IV. ADMINISTRATIVE GUIDELINES

A. Administration: For rectal administration only. Apply a water-soluble lubricant to administration tip prior to inserting.

B. Recommended for the visiting nurse to use C. Diff contact precautions including shoe covers, gown, face shield/mask, and gloves.

C. Do not allow the administration tube to sag or loop as this will prevent the entire dose from being delivered. Do not squeeze the bag to deliver fecal microbiota, live as this could be uncomfortable for the patient. Do not hang the bag from an IV pole. NOTE: Product temperature should be 2°C to 8°C or 36°F to 46°F at the time of fecal administration.

V. NURSING PROCEDURE

A. Supplies may include but are not limited to:

1. Water soluble lubricant
2. Shoe covers
3. Face shield
4. Protective gown
5. Mask
6. Disposable pad for patient to lay on
7. Administration set (provided with fecal microbiota, live)

B. Prescription items: (examples below)

1. Fecal microbiota, live bag (Rebyota) at refrigerated temperature (2˚C to 8˚C, 36˚F to 46˚F)

C. How Supplied:

1. Fecal microbiota, live and the administration set are shipped together in a freezer box. Each box may contain up to 6 cartons of fecal microbiota, live and up to 6 administration sets. Each carton (NDC 55566-9800-2) contains a single dose.

D. Storage and Handling:

1. Fecal microbiota, live contains live microorganisms. It is important to follow the storage requirements
2. **Upon Receipt**: Store the fecal microbiota, live carton in an ultracold freezer (-60˚C to -90˚C, -76˚F to -130˚F), or keep in original box up to 4 days. Alternatively, store in a refrigerator (2˚C to 8˚C, 36˚F to 46˚F) for up to 5 days (including thaw time). Do not refreeze fecal microbiota, live after thawing
3. Without an ultracold freezer, the time available until administration is 4 days in original freezer and 5 days refrigerated (including thaw time).
4. **Before Using:** Prior to use, thaw fecal microbiota, live completely by placing carton in a refrigerator (2˚C to 8˚C, 36˚F to 46˚F) for approximately 24 hours. Do not re-freeze fecal microbiota, live after thawing.

5. Store the administration set at 10°C to 34°C (50°F to 93°F). DO NOT store the administration set in the freezer.

E. Procedures:

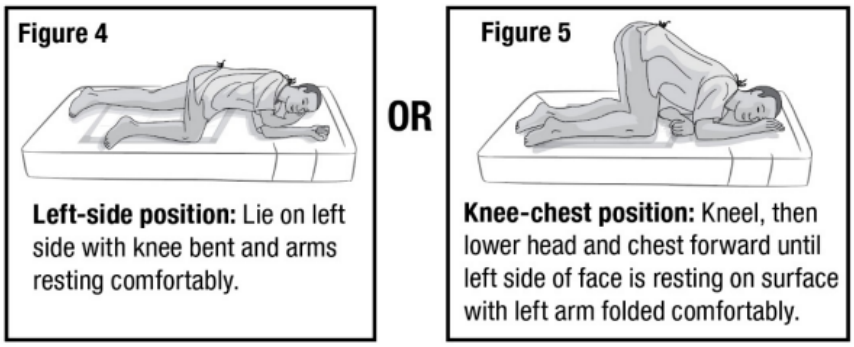
1. Don shoe covers, gown, face/mask cover, and gloves prior to entering the patient's home. Wash hands with soap and water before donning face mask with shield and a new pair of clean gloves

2. Explain the reasoning for visit and use of fecal microbiota, live, and ask when the patient had their last dose of antibiotic. Fecal microbiota, live should be administered 24-72 hours after last antibiotic dose.

3. Ensure product is in date from the time it was removed from ultra cold freezer (5 days refrigerated which includes the thaw time of 24 hours). Product should be at refrigerated temperature (2˚C to 8˚C, 36˚F to 46˚F)

4. Counsel patient on warnings, precautions, and potential side effects including but not limited to: anaphylaxis, abdominal pain/cramping, diarrhea, abdominal distension, flatulence, and nausea.

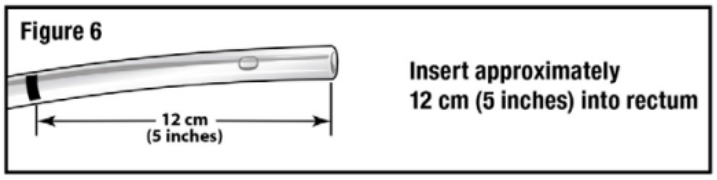
5. Prepare the patient for administration by requesting they empty their bladder and bowel, if possible. Place the patient in the left-side position or the knee-chest position with a disposable under pad beneath the patient



6. Open the administration set and close the pinch clamp by pushing the clamp until it is fully closed.

7. Remove the tab from the spike port of the bag containing thawed fecal microbiota, live and remove the cap from the administration tube spike. Insert the administration tube spike through the spike port of the bag containing thawed fecal microbiota, live. Do not remove air from the administration tube prior to insertion to avoid loss of fecal microbiota, live.

8. Apply water-soluble lubricant to the administration tube tip. Gently insert the administration tube tip into the rectum, about 12 cm (5 inches) in a direction pointed slightly toward the navel.



9. Hold the administration tube in place with one hand for the entire procedure to maintain the tube position in the rectum. With the other hand, open the pinch clamp on the administration tube, and then gradually raise the bag to allow delivery of the fecal microbiota suspension via gravity flow.

10. When the entire dose has been delivered, close the pinch clamp and then slowly withdraw the tube. Take care to prevent any residual fecal microbiota, live remaining in the tube from leaking out. Some fecal microbiota suspension will remain in the tube after administration.

11. Keep the patient in the left-side position or the knee-chest position for up to 15 minutes to minimize any cramping that may occur. There are no restrictions on the patient's use of the restroom.

12. Dispose of all components in medical waste. Double bag fecal microbiota, live bag and administration set and dispose in regular trash.

13. Post administration monitoring: Monitor patient and vital signs 15-30 minutes after administration is complete.

VI. CLINICAL MONITORING

A. Prior to therapy:

1. Assess patient allergy profile including food allergies
2. Ensure patient is completing antibiotics 24-72 hours prior to fecal microbiota, live is administered.

B. During therapy:

1. Assess for adverse effects including anaphylaxis, abdominal pain, abdominal cramping, distension, nausea, diarrhea, and flatulence.
2. Monitor for therapy efficacy and prevention of further C. Diff infections
3. Patients may start to see improvement right away or within 2 weeks of administration.
4. Patients should alert the managing physician if they have diarrhea 3 or more times a day for 2 days in a row

Please refer to the package insert for the most up to date guidance on this medication.

VII. REFERENCES:

Rebyota (fecal microbiota, live) [package insert].Roseville, MN: Rebiotix, Inc; 2022.

APPENDIX A: EPINEPRINE KIT INSTRUCTIONS FOR IM INJECTION

Emergency Medication After Your Infusion

Please call 1-800-755-4704 if you have any questions or concerns. We are available 24 hours a day, 7 days a week. In the event of an emergency, always call 911.

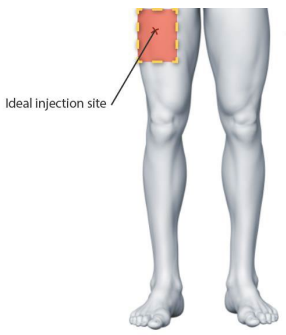
Your nurse will tell you when you need to use Emergency Medications.
Start with a clean work surface and clean hands.
Open the supply bag labeled Epinephrine Kit Contents.

1. **Remove 1 of each item**
    a. 1 -syringe
    b. 1 – brown labeled filter needle (BD Filter Needle)
    c. 1 – black labeled safety needle (Magellan Hypodermic Safety Needle 22G x 1")
    d. 1 ampule of epinephrine

Prepare IM (intramuscular) injection of Epinephrine:

2. **Attach the brown filtered needle to syringe**
    a. Be careful to not touch the tip of the syringe or the needle.
3. Using an **alcohol swab, wipe the neck of the epinephrine ampule**
4. Holding the ampule upright, **swirl and flick the ampule until all fluid flows to the bottom chamber** (the top chamber should be empty).
5. Using a new alcohol wipe, grasp the neck of the ampule and with your other hand grasp the bottom chamber of the ampule. **Quickly snap the top of the ampule off, directing the snap way from you.**
6. **Place the tip of the brown filter needle inside the ampule**. Tilting the ampule, **withdrawal all the medication into the syringe** by gently pulling back on the plunger. Be careful to not pull the plunger out of the syringe.
7. Remove the needle from the ampule and h**old the syringe upright** with the needle pointing upward. **Gently tap the side of the syringe to bring any air to the top of the syringe.**
8. **Push the air out of the syringe by gently pushing on the plunger**.
9. Replace the cap on the brown filter needle.
10. **Remove the brown filter needle and place the black safety needle onto the syringe.**

Give your IM Epinephrine injection



2. **Grasp your leg muscle at the outer mid-thigh** and **cleanse the area** with a new alcohol wipe.
3. **Push the needle into your leg muscle straight** in at a 90-degree angle.
4. **Inject the medication** by depressing the plunger in a slow and steady motion.
5. **Remove the needle** and wipe the site with the alcohol wipe.

Place all trash in the bag and take with you when you seek medical care. **Give the bag to the nurse or EMT**, so your doctor will know what medication you already took. They will properly dispose of the syringe and needles.

Call 911 or have someone drive you to the emergency department.