OPENBIOME

FMT Capsule DE

with MEM Technology Microbiota Preparation

FMPCapDE

CLINICIAN'S CHECKLIST

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FMT Capsule DE

Clinician's Checklist

Clinician's checklist for the administration of 30 capsules of FMT Capsule DE (1 dose) orally for recurrent *Clostridioides difficile* infection (rCDI)

Patient preparation

1. Review Indications & Contraindications

- ☐ Confirm that the indication to be treated by Fecal Microbiota Transplantation (FMT) is *C. difficile* infection (CDI) that is not responsive to standard therapy, and rule out alternative diagnosis (e.g. post-infectious IBS, inflammatory bowel disease, celiac disease).
    - **For fulminant (previously referred to as severe or severe-complicated CDI):** We suggest that clinicians treating severe or severe-complicated CDI by FMT consider a colonoscopic administration and review the protocols detailed in M. Fischer et al., "Faecal microbiota transplantation plus selected use of vancomycin for severe-complicated Clostridium difficile infection: Description of a protocol with high success rate," Aliment Pharmacol Ther. 2015;42(4):470-476.

- ☐ Review contraindications for FMT material administered orally, including but not limited to:
  - Dysphagia: oropharyngeal, esophageal, functional, neuromuscular (e.g. stroke, multiple sclerosis, ALS), or evidence of dysphagia when the 'safety test' capsule(s) are administered
  - History of aspiration
  - History of gastroparesis
  - History of intestinal obstruction
  - Fulminant (previously referred to as severe or severe-complicated) *Clostridioides difficile* infection, given high ileus risk
  - Severe food allergy (e.g. anaphylaxis or anaphylactoid reaction)
  - Adverse event attributable to a previous FMT
  - Allergies to sodium chloride, glycerol, theobroma oil, hide bovine gelatin, sodium lauryl sulfate, colorants FD&C, or titanium dioxide, all ingredients Generally Recognized As Safe (GRAS)
  - History of ongoing antibiotic use (e.g. nitrofurantoin for UTI prophylaxis)
  - Any condition for which the treating physician thinks the treatment may pose a health risk (e.g. severely immunocompromised)

Warnings:

OpenBiome cannot guarantee the inclusion or exclusion of any food allergens (e.g. tree nuts, seafood) from a donor's diet. This material has not been screened for CMV and EBV and should not be used for patients at risk for CMV- or EBV-associated diseases (e.g., severely immunocompromised patients such as seronegative transplant recipients). FMT carries the risk of known and unknown infectious disease transmission and potentially microbiome-mediated diseases. The risk of aspiration (via naso-enteric administration), bacteremia, and death have been reported in the literature.

2. Obtain Informed Consent

☐ Inform patients of the risks, benefits, and treatment alternatives for FMT in general

☐ Inform patients of the risks, benefits, and treatment alternatives for FMT Capsule DE.

☐ Inform the patient that the use of FMT to treat recurrent *C. difficile* infection (rCDI) is investigational.

3. Administer safety test capsule

☐ Patients must ingest 1 placebo 'safety test' capsule (included with each treatment) under direct observation of a physician. Any clinical concerns suggesting an aspiration risk is an absolute contraindication to capsule administration.

4. Review Medications

☐ Discontinue anti-rCDI antibiotics (e.g. vancomycin, fidaxomicin) 48 hours prior to FMT Capsule DE administration. Concomitant use of other antibiotics could reduce the procedure's efficacy.

☐ Antiemetic medications are not recommended for routine administration.

5. Day of FMT Capsule DE administration

☐ Patients should maintain a clear liquid diet the day of FMT Capsule DE administration.

☐ Patients should fast (NPO) for 2 hours prior to the FMT Capsule DE administration.

Administration

- ☐ Capsules must be administered under direct observation by a physician.
- ☐ Capsules must be kept frozen until ready for administration.
- ☐ When ready for administration, remove capsules from freezer, confirm that the capsules are not expired, and note the time that they are removed.
- ☐ Open bottle and remove cotton immediately.
- ☐ Empty capsules from bottle into a sterile container. A clean K-basin or equivalent container should be used.
- ☐ Provide the patient with plenty of clear liquid to drink during administration.
- ☐ All 30 FMT Capsule DE pills should be ingested within 90 minutes after extraction from the freezer.

Post Administration

- ☐ Patients should fast (NPO) for 1 hour after the administration of FMT Capsule DE.
- ☐ Patients may return to a full diet following post-administration fasting.

Adverse Reactions

This is a summary of adverse reactions reported in peer-reviewed literature but may not be not be a comprehensive list. Please consult the primary sources listed in the references section of the OpenBiome Clinical Primer for more detailed information. Procedure-related adverse events (e.g. aspiration) are beyond the scope of this document.

- ☐ **Common, mild adverse events**: transient diarrhea (70%), transient abdominal cramps/discomfort (20%) and nausea (<5%) in 24 hours post-FMT. Transient fever, bloating, belching, vomiting, and borborygmus have also been reported. Constipation (20%), excess flatulence (25%) have been reported in follow-up. There is also a theoretical risk of small intestinal bacterial overgrowth.
- ☐ **Rare, serious adverse events**: The following risks should be considered:
    - ***Infection*:** Although this material has been screened for bacteria, viruses, fungi and parasites, there is a risk of transmission of known and unknown infectious organisms contained in the donor stool. Post-FMT bacteremia (e.g. *E. coli*, *Klebsiella*), sepsis and fatal

events may rarely occur.

- ***Inflammatory bowel disease (IBD) flare*** in those with underlying IBD.
- ***Allergy/Anaphylaxis*** to antigens in donor stool.
- ***Non-infectious disease transmission*:** There is a theoretical risk of developing disease that may be related to donor gut microbiota. These include obesity, metabolic syndrome, cardiovascular disease, autoimmune conditions, allergic/atopic disorders, neurologic disorders, psychiatric conditions and malignancy. Persons with these known conditions are excluded from donating stool to OpenBiome.
- ***Aspiration:*** Capsule administration carries a risk of aspiration (see “Indications & contraindications”).

Mandatory Clinical Follow-Up

- ☐ Assess patients 8 weeks after FMT administration (phone/clinic visit) for clinical cure (e.g. absence of 3 or more liquid bowel movements a day).
- ☐ Complete the mandatory Material Tracking Log and FMT Follow-Up Form included with your shipment.
- ☐ Send Material Tracking Log and FMT Follow-Up Form by email to safety@openbiome.org or by fax to (617) 575-2201, reporting de-identified patient outcomes.

This quality assurance data is critical to our efforts to guard against potential threats to the safety and efficacy of FMT, and your participation is a strict condition for receiving future supplies of FMT Capsule DE

Post-FMT Patient Counseling

Advise patient to thoroughly clean their home to avoid reinfection after FMT. When cleaning, the patient should:

- ☐ Use an Environmental Protection Agency (EPA)-registered disinfectant with a *C. difficile*-sporidical label claim, such as household bleach.
- ☐ Scrub high-touch surface areas such as toilets, faucets, and showers.
- ☐ Wear disposable gloves when cleaning; wash hands with soap and water thoroughly afterwards.
- ☐ Consult OpenBiome's Patient Education materials, which can be found on our website: www.openbiome.org/patient-support.

Important Reminders

- FMT Capsule DE must be stored in a medical-grade freezer at -20°C or colder at all times, and should never be refrozen.
- FMT Capsule DE that has been removed from the freezer for administration to a patient should be disposed of if not consumed within 90 minutes.

Ingredients

Frozen human fecal microbiota filtered to 330 microns, theobroma oil, glycerol, hide bovine gelatin, sodium lauryl sulfate, colorants FD&C, titanium dioxide, interior gelatin capsule, external acid-resistant capsule

CAUTION

New Drug—Limited by Federal (or United States) law to investigational use. Immediately report any adverse events to https://www.openbiome.org/adverse-events.

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CONTACT INFORMATION

Safety & Adverse Events
safety@openbiome.org
(617) 575-2201 x 9

General
info@openbiome.org
(617) 575-2201