

Clinical Policy: Fecal Bacteriotherapy

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Description

Fecal bacteriotherapy is also known as fecal biotherapy, fecal microbiota transplantation (FMT), stool or fecal transplant, fecal transfusion, fecal enema or human probiotic infusion. This procedure refers to the process of transplantation of fecal bacteria from a healthy individual into a recipient as a treatment for those suffering from clostridium difficile infection (CDI), which produces effects ranging from diarrhea to pseudomembranous colitis.

Policy/Criteria

- I. It is the policy of Health Net of California that fecal bacteriotherapy may be considered medically necessary as a treatment for recurrent or relapsing CDI when the following criteria are met:
 - a. Infection confirmed by a positive stool test for Clostridium difficile toxin,
 - b. There have been at least 3 episodes of mild to moderate, or 2 episodes of severe recurrent Clostridium difficile infection and associated diarrhea refractory to appropriate antibiotic therapy,
 - c. Patient is not immunocompromised

- II. It is the policy of Health Net of California that fecal bacteriotherapy is investigational for any other indication as there is a paucity of peer-reviewed literature and lack of long-term outcomes regarding safety and efficacy.

Background

CDI is one of the leading causes of nosocomial gastroenteritis in the United States, particularly among hospitalized patients ≥ 65 years of age. Given the challenges in managing recurrent CDI, including increased risk of severe complications, nonpharmacological approaches, including FMT, have been used.

FMT may be administered via oral capsules, lower gastrointestinal (GI) tract procedure (colonoscopy, retention enema), or upper GI tract procedure (nasojejunal /nasoduodenal tube). The choice is based in part on clinical circumstances, available options, and patient preference. Infusion of FMT involves the instillation of saline-diluted fecal matter from the specified donor, via a nasoduodenal tube, retention enema, or colonoscope, into the colon of a patient with recurrent CDI and associated diarrhea. Rigorous screening of candidate stool donors for occult pathogens is important to minimize the risk of infection. Donors must be tested for a wide array of bacterial and parasitic infections. The fecal transplant material is then prepared and administered in a clinical environment to ensure that precautions are taken. Transplantation of fresh donated feces is recommended to take place within 24 hours.

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Various moderate quality studies were done, including randomized controlled trials, systematic reviews, case studies and retrospective observational studies. They noted that FMT cures a large proportion of patients with refractory or recurrent CDI who had failed ≥ 1 course of standard antibiotic treatment. FMT is generally well tolerated but adverse events may occur such as procedural events, abdominal discomfort and infections from stool donors that were undetected at the time of screening.

American Gastroenterology Association (AGA)

The American Gastroenterological Association (AGA) Institute, in partnership with other organizations and with funding from the National Institutes of Health, has developed the prospective FMT National Registry to assess FMT. The investigators report the results from the first 259 patients collected from 20 different sites. Of the first 259 participants enrolled at 20 sites, 222 have completed short-term follow-up at 1 month, and 123 have follow-up to 6 months; 171 (66%) are female. All FMTs were done for CDI, and 249 (96%) used an unknown donor (e.g., stool bank). One-month cure occurred in 200 (90%); of these, 197 (98%) received only a single FMT. Among 112 with initial cure who were followed to 6 months, 4 (4%) had CDI recurrence. Severe symptoms reported within 1-month of FMT included diarrhea (5 (2%)) and abdominal pain (4 (2%)); 3 (1%) had hospitalizations possibly related to FMT. At 6 months, new diagnoses of irritable bowel syndrome were made in 2 (1%) and inflammatory bowel disease in 2 (1%). The authors concluded that “this prospective real-world study demonstrated high effectiveness of FMT for CDI with a good safety profile. Assessment of new conditions at long-term follow-up is planned as this registry grows and will be important for determining the full safety profile of FMT.”

The 2019 AGA guidelines on the management of patients with mild-to-moderate ulcerative colitis (UC) without *Clostridium difficile* infection recommend fecal microbiota transplantation be performed only in the context of a clinical trial. The use of FMT for treatment of UC should be considered experimental at this time. Current evidence was rated as very low because only small, noncomparative cohort studies of heterogeneous patients have been completed. AGA noted that large studies with long-term follow-up are needed

National Institute for Health and Care Excellence

Current evidence on FMT for recurrent CDI that has failed to respond to antibiotics and other treatments shows that it is efficacious in reducing symptoms. Therefore the procedure may be used provided that normal arrangements are in place for clinical governance, consent and audit.

American College of Gastroenterology

The American College of Gastroenterology 2021 guidelines favor administration of FMT via colonoscopy or oral capsules, with delivery by enema if other methods are unavailable. The ACG recommends that FMT be considered for patients with severe and fulminant CDI unresponsive to antibiotic therapy. For recurrent CDI, FMT is recommended for patients experiencing a second or further recurrence with delivery through colonoscopy or capsules. Repeat FMT is suggested if the patient experiences a recurrence of CDI within eight weeks of an initial FMT. For patients with inflammatory bowel disease (IBD) and recurrent CDI, FMT should be considered. The panel recommends that immunocompromised patients be tested for

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CMV and EBV prior to undergoing FMT and if seronegative be advised of the risks, benefits, and alternatives (including patient-selected donor use). They conclude that FMT has emerged as an effective treatment, but questions remain regarding best method of delivery, optimal donor screening, and long-term safety of the procedure (Kelly et al., 2021).

Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA) (2018)

Fecal microbiota transplantation is recommended as an option for patients with multiple recurrences of CDI who have failed appropriate antibiotic treatments [following an initial treatment of CDI and two recurrences (i.e. after three treated CDI episodes) that have been non-responsive to at least two regimens of antibiotics (i.e., various combinations of vancomycin, fidaxomicin, and/or metronidazole] (*strong recommendation, moderate quality of evidence*). It also notes to Consider fecal microbiota transplantation for pediatric patients with multiple recurrences of CDI following standard antibiotic treatments (*weak recommendation, very low quality of evidence*).

In a June 2019 Safety Communication, the Food and Drug Administration (FDA) informed health care providers and patients of the potential risk of serious or life-threatening infections with the use of fecal microbiota for transplantation (FMT). The agency was made aware of bacterial infections caused by multi-drug resistant organisms (MDROs) that have occurred due to transmission of a MDRO from use of investigational FMT. Two immunocompromised adults who received investigational FMT developed invasive infections caused by extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* (*E.coli*). One of the individuals died. The FDA recommends donor screening, testing of donor stool and exclusion for stool that test positive for MDRO.

The FDA also issued a safety warning in March 2020: FDA is informing health care providers and patients of the potential risk of serious or life-threatening infections with the use of fecal microbiota for transplantation (FMT). The FDA is now aware of infections caused by enteropathogenic *Escherichia coli* (EPEC) and Shigatoxin-producing *Escherichia coli* (STEC) that have occurred following investigational use of FMT that it suspects are due to transmission of these pathogenic organisms from FMT product supplied by a stool bank company based in the United States. The stool bank provides FMT product manufactured from pre-screened donors to healthcare providers and researchers.

In August 2022, the US Food and Drug Administration (FDA) issued guidance to reduce the risk of transmission of monkeypox virus through fecal microbiota transplants (FMT). The recommended measures include screening donors with questions directed at identifying those at high risk for monkeypox and those with recent or active monkeypox virus infection, developing exclusion criteria to exclude donors with a positive questionnaire screen, and providing informed consent to all FMT recipients regarding the possible risk of monkeypox virus transmission via FMT.

Coding Implications

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CPT® Codes	Description
44705	Preparation of fecal microbiota for instillation, including assessment of donor specimen

HCPCS Codes	Description
G0455	Preparation with instillation of fecal microbiota by any method, including assessment of donor specimen

ICD-10-CM Code	Description
A04.7	Enterocolitis due to Clostridium difficile

Reviews, Revisions, and Approvals	Date	Approval Date
Policy Adopted from Health Net NMP#519, Fecal Bacteriotherapy	11/16	
Policy update – no changes	11/17	11/17
Criteria revised based on 2017 guidelines from the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America	11/18	11/18
Added FDA safety recommendations to background section	11/19	11/19
Revised Ib to add.. or 2 episodes of severe.. Added FDA safety warning, FMT National Registry information, added references	11/20	11/20
Clarified recommendation from ACG, Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA) but no change in criteria. Updated references	11/21	11/21
Added information to background of the various methods of administration, added section regarding FDA caution for screening donor for monkeypox (FDA March 22), Updated references	11/22	11/22

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Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

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Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at <http://www.cms.gov> for additional information.

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Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA):

In 2021, IDSA and SHEA updated the 2018 clinical practice guidelines for the diagnosis and treatment of clostridium difficile infection in adults. The Societies recommended pharmacotherapy using vancomycin, fidaxomicin, and/or metronidazole depending on availability of medications. Adjunctive bezlotoxumab is recommended depending on the episode and the severity of the C difficile. The strength of the recommendations were conditional and the quality of evidence ranged from low to moderate. The Societies' recommendations for the treatment of Clostridiodes difficile infection in adults included the following:

- Initial CDI episode: – Recommended and Alternative Treatments: – Preferred: fidaxomicin 200mg given twice daily for 10 days (implementation remains dependent on available resources). – Alternative: vancomycin 125mg given four times daily by mouth for 10 days. – Alternative for nonsevere CDI if the above are unavailable: Metronidazole 500mg three times daily by mouth for 10-14 days. Page 18 of 29 Medical Coverage Policy: 0516
- First CDI recurrence: – Preferred: fidaxomicin 200 mg given twice daily for 10 days, or twice daily for five days followed by once every other day for 20 days – Alternative: vancomycin 125 mg given four times daily by mouth for 10 days. – Adjunctive: bezlotoxumab 10mg/kg intravenous (IV) once during administration of SOC antibiotics. In patients with risk factors for CDI recurrence (such as age \geq 65 years, immunocompromised per history or use of immunosuppressive therapy, and severe CDI on presentation) may particularly benefit from receiving bezlotoxumab
- Second or subsequent CDI recurrence: – Preferred: fidaxomicin 200 mg given twice daily for 10 days, OR twice daily for five days followed by once every other day for 20 days – Alternative: vancomycin by mouth in a tapered and pulsed regimen for 10 days, OR vancomycin 125 mg given four times daily by mouth for 10 days followed by Rifaximin 400mg three times daily for 20 days. – Adjunctive: bezlotoxumab 10 mg/kg IV once during administration of SOC antibiotics (caution for use in patients with history of congestive heart failure). – Note: The panel recommends treatment with appropriate antibiotic regimens for at least two recurrences (i.e., three CDI episodes) prior to offering fecal microbiota transplantation.
- Fulminant CDI: (definition is supported by hypotension, shock, ileus, megacolon) – Vancomycin 500mg four times daily by mouth or by nasogastric tube. – If ileus, consider adding rectal instillation of vancomycin. – Intravenously administered Metronidazole (500mg every eight hours) should be administered together with oral or rectal vancomycin, particularly if ileus is present. FMT is recommended only for patients with multiple recurrences of CDI and failure on appropriate antibiotic treatments. Appropriate screening of donor and donor fecal specimens, in accordance with FDA recommendations, is essential.