Clinical Policy: Fecal Bacteriotherapy

Reference Number: HNCA.CP.MP.519
Effective Date: 11/16
Last Review Date: 11/21

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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 involves infusions of 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. 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.

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. Adverse reactions were generally rare.

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 are 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 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 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).

European Society of Clinical Microbiology and Infectious Diseases

For multiple recurrent CDI unresponsive to repeated antibiotic treatment, FMT is strongly recommended in combination with oral antibiotic treatment.

UpToDate

Recurrent and severe CDI despite antibiotic therapy is increasingly common. Restoration of the normal fecal microbiota may be important for resolving infection refractory to oral metronidazole or vancomycin. FMT offers a means to durably restore the normal microbiota. It is recommended that FMT be done at a center of expertise in patients with recurrent CDI who have failed multiple courses of antibiotic therapy (Grade 1B).

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*). 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.

Coding Implications
This clinical policy references Current Procedural Terminology (CPT®). CPT® is a registered trademark of the American Medical Association. All CPT codes and descriptions are copyrighted 2015, American Medical Association. All rights reserved. CPT codes and CPT descriptions are from the current manuals and those included herein are not intended to be all-inclusive and are included for informational purposes only. 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.

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

References

1. Agrawal M,, Aroniadis OC, Brandt LJ, et al. The Long-term Efficacy and Safety of Fecal Microbiota Transplant for Recurrent, Severe, and Complicated Clostridium difficile Infection in 146 Elderly Individuals. 1. J Clin Gastroenterol. August 26, 2015.
2. American College of Gastroenterology (ACG). Prevention, diagnosis, and treatment of Clostridioides difficile infections. May 2021. Accessed Sept 29, 2021. Available at URL address: https://gi.org/guidelines/
3. American College of Gastroenterology Guidelines for Diagnosis, Treatment, and Prevention of Clostridium difficile Infections. (2013) Available at: http://gi.org/guideline/diagnosis-and-management-of-c-difficile-associated-diarrhea-and-colitis/
4. American Gastroenterological Association. Clinical Practice Guidelines. AGA clinical practice Sept 30, 2021. Available at URL address: https://www.gastro.org/guidelines/ibd-and-bowel-disorders.
5. Aroniadis OC, Brandt LJ, Greenberg A et al. Long-term Follow-up Study of Fecal Microbiota Transplantation for Severe and/or Complicated Clostridium difficile Infection: A Multicenter Experience. J Clin Gastroenterol. 2015 Jun 23.

6. Borody TJ, Leis S, Pang G, et al. Fecal microbiota transplantation in the treatment of recurrent Clostridium difficile infection. UpToDate. Sept 2021.
7. Cammarota G, Masucci L, Ianiro G, et al. Randomised clinical trial: faecal microbiota transplantation by colonoscopy vs. vancomycin for the treatment of recurrent Clostridium difficile infection. Aliment Pharmacol Ther. 2015;41(9):835-843.
8. Debast SB, Bauer MP, Kuijper EJ. European Society of Clinical Microbiology and Infectious Diseases: update of the treatment guidance document for Clostridium difficile infection. Clin Microbiol Infect. 2014;20 (Suppl 2):1-26.
9. ECRI Institute. Fecal Microbiota Transplantation for Treating Irritable Bowel Syndrome. Plymouth Meeting (PA): ECRI Institute; 2020 Jul 01. (Custom Rapid Responses).
10. Fecal Microbiota for Transplantation: Safety Communication- Risk of Serious Adverse Reactions Due to Transmission of Multi-Drug Resistant Organisms. Available at: https://www.fda.gov/safety/medical-product-safety-information/fecal-microbiota-transplantation-safety-communication-risk-serious-adverse-reactions-due
11. Food and Drug Administration (FDA). Fecal Microbiota Transplantation: Safety Communication - Risk of Serious Adverse Reactions Due to Transmission of Multi-Drug Resistant Organisms. 2019;
12. Hayes. Health Technology Brief. Fecal Microbiota Transplant for Refractory or Recurrent Clostridium Difficile Infection in Adults. October 2018 Update
13. Kelly CR, Fischer M, Allegretti JR, LaPlante K, Stewart DB, Limketkai BN, Stollman NH. ACG Clinical Guidelines: Prevention, Diagnosis, and Treatment of Clostridioides difficile Infections. Am J Gastroenterol. 2021 Jun 1;116(6):1124-1147
14. Kelly CR, Ihunnah C, Fischer M, et al. Fecal microbiota transplant for treatment of clostridium difficile infection in immunocompromised patients.
15. Kelly, CR, Yen, EF et al , Fecal Microbia Transplantation is Highly Effective in Real-World Practice: Initial Results from the FMT National Registry, Published:October 01, 2020 DOI:https://doi.org/10.1053/j.gastro.2020.09.038
16. Lee CH, Chai J, Hammond K et al. Long-term durability and safety of fecal microbiota transplantation for recurrent or refractory Clostridioides difficile infection with or without antibiotic exposure. Eur. J. Clin. Microbiol. Infect. Dis., 2019 Jun 6;38(9). PMID 31165961
17. McDonald, LC, Gerding DN et al. Clinical Practice Guidelines for Clostridium difficile Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA) Clinical Infectious Diseases, Volume 66, Issue 7, 19 March 2018, Pages e1–e48, https://doi.org/10.1093/cid/cix1085
18. Mullish, BH et al The use of faecal microbiota transplant as treatment for recurrent or refractory Clostridium difficile infection and other potential indications: joint British Society of Gastroenterology (BSG) and Healthcare Infection Society (HIS) guidelines. Journal of Hospital Infection 100 (2018) S1eS31
19. National Institute for Health and Care Excellence (NICE). Faecal microbiota transplant for recurrent Clostridium difficile infection [IPG485]. 2014. Available at: https://www.nice.org.uk/Guidance/IPG485
20. Tariq R, Pardi DS, Bartlett MG et al. Low Cure Rates in Controlled Trials of Fecal Microbiota Transplantation for Recurrent Clostridium difficile Infection: A Systematic Review and Metaanalysis. Clin. Infect. Dis., 2019 Apr 9;68(8). PMID 30957161

21. van Nood E, Vrieze A, Nieuwdorp M, et al. Duodenal infusion of donor feces for recurrent Clostridium difficile. N Engl J Med. 2013;368(5):407-415.
22. Zhou HY, Guo B, Lufumpa E, et al. Comparative of the Effectiveness and Safety of Biological Agents, Tofacitinib, and Fecal Microbiota Transplantation in Ulcerative Colitis: Systematic Review and Network Meta-Analysis. Immunol Invest. Feb 02 2020: 1-15. PMID 32009472

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 Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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.