MEDICAL POLICY

SUBJECT: FECAL BACTERIOTHERAPY	EFFECTIVE DATE: 08/16/12 REVISED DATE: 08/15/13, 07/17/14, 07/16/15, 06/16/16, 06/15/17, 09/20/18
POLICY NUMBER: 2.01.48 CATEGORY: Technology Assessment	PAGE: 1 OF: 7

- ***If a product excludes coverage for a service, it is not covered, and medical policy criteria do not apply.***
- ***If a commercial product (including an Essential Plan product) or a Medicaid product covers a specific service, medical policy criteria apply to the benefit.***
- ***If a Medicare product covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit.***

POLICY STATEMENT:

I. Based upon our criteria and assessment of peer-reviewed literature, fecal bacteriotherapy has been medically proven to be effective and is considered **medically appropriate** for the treatment of recurrent clostridium difficile infection (CDI) when ALL of the following have been met:
   A. Patient has had at least three episodes of recurrent CDI despite the standard antibiotic therapy;
   B. Patient is not immunocompromised; AND
   C. The appropriate donor stool screening has been completed (see guidelines below).

II. Based upon our criteria and assessment of the peer-reviewed literature, fecal bacteriotherapy has not been medically proven to be effective and is considered **investigational** for all other indications, including but not limited to, the first line treatment for CDI or the treatment of inflammatory bowel disease.

POLICY GUIDELINES:

I. The most appropriate donor is a spouse, significant other, or first degree relative if possible. Donor stool screening should follow the FDA guidelines for biologic donors and include at least the following:
   A. Screening for transmissible bloodborne diseases or other diseases associated with microflora changes (e.g., irritable bowel syndrome, constipation);
   B. Screening for transmissible pathogens;
   C. Donor has not had antibiotic therapy for at least three months previous to donation; and
   D. Donor should not ingest foods that the patient is allergic to.

II. The Federal Employee Health Benefit Program (FEHBP/FEP) requires that procedures, devices or laboratory tests approved by the U.S. Food and Drug Administration (FDA) may not be considered investigational and thus these procedures, devices or laboratory tests may be assessed only on the basis of their medical necessity.

DESCRIPTION:

The recurrence of Clostridium difficile infection (CDI) is one of the most difficult and increasingly common challenges associated with the infection. An initial incidence of CDI is followed by a relapse within 30 days in about 20 – 30 % of cases, and the risk of recurrence doubles after two or more occurrences. Older age, intercurrent antibiotic use for non- *C.* difficile indications, renal insufficiency, immune deficiency and antacid medications are some of the known risk factors for recurrence. The presence of just three clinical criteria: age greater than 65 years, severe disease, and continued use of antibiotics after treating the initial CDI episode, are predictive of an almost 90 % relapse rate. It is now recognized that the presence of normal, healthy, intestinal microbiota offers protection against CDI. Conversely, severe disruption of normal intestinal microbiota by repeated cycles of antibiotics, including metronidazole and vancomycin that are used to treat CDI, is likely one of the major reason for its recurrence.

The American College of Gastroenterology published guidelines for the diagnosis, treatment, and prevention of CDI in 2013. Highlights of the guidelines for the treatment of CDI are as follows: Patients with mild-to-moderate CDI should be treated with metronidazole 500 mg orally three times per day for 10 days (Strong recommendation, high-quality evidence); Patients with severe CDI should be treated with vancomycin 125 mg four times daily for 10 days (Conditional recommendation, moderate-quality evidence); Failure to respond to metronidazole therapy within 5 – 7 days should prompt consideration of a change in therapy to vancomycin at standard dosing (Strong recommendation, moderate-quality evidence); For mild-to-moderate CDI in patients who are intolerant/allergic to metronidazole and for pregnant /breastfeeding women, vancomycin should be used at standard dosing. (Strong recommendation, high-quality evidence);

In patients in whom oral antibiotics cannot reach a segment of the colon, such as with Hartman's pouch, ileostomy, or colon diversion, vancomycin therapy delivered via enema should be added to treatments above until the patient improves (Conditional recommendation, low-quality evidence). Vancomycin delivered orally (125 mg four times per day) plus intravenous metronidazole (500 mg three times a day) is the treatment of choice in patients with severe and complicated CDI who have no significant abdominal distention (Strong recommendation, low-quality evidence). Vancomycin delivered orally (500 mg four times per day) and per rectum (500 mg in a volume of 500 ml four times a day) plus intravenous metronidazole (500 mg three times a day) is the treatment of choice for patients with complicated CDI with ileus or toxic colon and /or significant abdominal distention (Strong recommendation, low-quality evidence). The first recurrence of CDI can be treated with the same regimen that was used for the initial episode. If severe, however vancomycin should be used. The second recurrence should be treated with a pulsed vancomycin regimen (Conditional recommendation, low-quality evidence). If there is a third recurrence after a pulsed vancomycin regimen, fecal microbiota transplant (FMT) should be considered (Conditional recommendation, moderate-quality evidence).

Fecal bacteriotherapy, also known as fecal microbiotia therapy (FMT) and fecal transplantation, involves restoration of normal bowel flora by introducing bacterial flora by the infusion of a stool preparation obtained from of a healthy stool donor, who in most instances is a close relative. Fecal bacteriotherapy involves single to multiple infusions and can be carried out via different routes such as nasogastric tube, enema, or more commonly by through a colonoscope. The proposed benefits of fecal bacteriotherapy include the restoration of the colonic flora to its natural state by replacing the missing Bacteroidetes and Firmicutes species, the eradication of C. difficile, and the resolution of the debilitating clinical symptoms such as diarrhea, cramping and urgency.

The principal potential risk associated with fecal bacteriotherapy is transmission of contagious agents contained in the donor stool. There are risks of transmitting agents that do not cause a disease immediately after transplantation, but may complicate the treatment of the patient in the future. The fecal transplant material needs to be prepared and administered in a clinic or hospital environment to ensure that necessary precautions are followed and the donor stool must be appropriately screened for infectious diseases and pathogens. The FDA guidelines for donors of human cells, tissues and cellular and tissue-based products should be reviewed. Stool testing would include: C difficile toxin; routine bacterial culture for enteric pathogens; fecal Giardia antigen; fecal Cryptosporidium antigen; acid- fast stain for Cyclospora and Isospora (acid-fast for cryptosporidium if no antigen is available); ova and parasites; and Heliobacter pylori fecal antigen. Serologic testing should include the following: HIV (type I and II); Testing for hepatitis A, B and C; and rapid plasma regain (PR) and florescent treponemal antibody absorption test (FTA-ABS) for syphilis.

RATIONALE:

Based on the outcomes published from case series/case reports, and one randomized controlled trial, fecal bacteriotherapy is a highly effective therapy for refractory, recurrent C Difficile infection when standard treatments have failed. Overall, fecal bacteriotherapy resulted in resolution for 92% of patients (89% after a single treatment). Safety-wise, relapses and deaths after fecal bacteriotherapy were relatively uncommon; however, longer-term outcomes are needed to ensure these complication rates do not increase. Fecal bacteriotherapy as a first line therapy for C Difficile infection as not been studied sufficiently as the participants in published studies thus far have been patient who have failed multiple antibiotic regimens.

FMT has been shown to have some effect in alleviating symptoms in other difficult-to-treat conditions such as irritable bowel syndrome, and inflammatory bowel diseases such as Crohn's disease and ulcerative colitis. The majority of studies in these diseases mainly consist of case series, case reports, and cohort studies. While outcome data are promising, there is insufficient evidence at this time to implement FMT as a treatment regimen. Additional RCTs and longer-term studies are still needed to determine efficacy and safety profiles for patients with diseases other than recurrent C Difficile infection.

CODES: Number Description

Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.

CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.

Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.

CPT:	44705	Preparation of fecal microbiota for instillation, including assessment of donor specimen

HCPCS:	G0455	Preparation with instillation of fecal microbiota by any method, including assessment of donor specimen
ICD10:	A04.7	Enterocolitis due to Clostridium

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* key article

KEY WORDS:

Fecal microbiota therapy (FMT), Fecal transfusion, Fecal transplant, Human probiotic infusion (HPI), Intestinal microbiotia Transplantation (IMT), Microbiome, Stool transplant

CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS

Based upon our review, fecal bacteriotherapy is not addressed in National or regional CMS coverage determinations or policies.