



CLINICAL PAYMENT AND CODING POLICY

If a conflict arises between a Clinical Payment and Coding Policy (CPCP) and any plan document under which a member is entitled to Covered Services, the plan document will govern. If a conflict arises between a CPCP and any provider contract pursuant to which a provider participates in and/or provides Covered Services to eligible member(s) and/or plans, the provider contract will govern. "Plan documents" include, but are not limited to, Certificates of Health Care Benefits, benefit booklets, Summary Plan Descriptions, and other coverage documents. BCBSTX may use reasonable discretion interpreting and applying this policy to services being delivered in a particular case. BCBSTX has full and final discretionary authority for their interpretation and application to the extent provided under any applicable plan documents.

Providers are responsible for submission of accurate documentation of services performed. Providers are expected to submit claims for services rendered using valid code combinations from Health Insurance Portability and Accountability Act (HIPAA) approved code sets. Claims should be coded appropriately according to industry standard coding guidelines including, but not limited to: Uniform Billing (UB) Editor, American Medical Association (AMA), Current Procedural Terminology (CPT®), CPT® Assistant, Healthcare Common Procedure Coding System (HCPCS), ICD-10 CM and PCS, National Drug Codes (NDC), Diagnosis Related Group (DRG) guidelines, Centers for Medicare and Medicaid Services (CMS) National Correct Coding Initiative (NCCI) Policy Manual, CCI table edits and other CMS guidelines.

Claims are subject to the code edit protocols for services/procedures billed. Claim submissions are subject to claim review including but not limited to, any terms of benefit coverage, provider contract language, medical policies, clinical payment and coding policies as well as coding software logic. Upon request, the provider is urged to submit any additional documentation.

Fecal Analysis in the Diagnosis of Intestinal Dysbiosis and Fecal Microbiota Transplant Testing

Policy Number: CPCPLAB025

Version 1.0

Enterprise Medical Policy Committee Approval Date: 1/25/2022

Plan Effective Date: May 1, 2022

Description

BCBSTX has implemented certain lab management reimbursement criteria. Not all requirements apply to each product. Providers are urged to review Plan documents for eligible coverage for services rendered.

Reimbursement Information:

1. Fecal analysis by culture prior to fecal microbiota transplant (FMT) for the following microorganisms **may be reimbursable**:
 - a. Extended spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae
 - b. Vancomycin-resistant Enterococci (VRE)
 - c. Carbapenem-resistant Enterobacteriaceae (CRE)
 - d. Methicillin-resistant Staphylococcus aureus (MRSA)
 - e. Campylobacter
 - f. Shigella
 - g. Salmonella
2. Fecal analysis by nucleic acid amplification testing (NAAT) prior to fecal microbiota transplant (FMT) for the following microorganisms **may be reimbursable**.
 - a. C. Difficile
 - b. Campylobacter
 - c. Salmonella
 - d. Shigella
 - e. Shiga toxin-producing Escherichia coli
 - f. Norovirus
 - g. Rotavirus
 - h. COVID-19 (SARS-CoV-2)
3. Fecal analysis by nucleic acid amplification testing (NAAT) prior to fecal microbiota transplant (FMT) for the following microorganisms **is not reimbursable**:
 - a. Extended spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae
 - b. Vancomycin-resistant Enterococci (VRE)
 - c. Carbapenem-resistant Enterobacteriaceae (CRE)
 - d. Methicillin-resistant Staphylococcus aureus (MRSA)
 - e. Any other microorganisms not listed above
4. Fecal analysis of the following components **is not reimbursable** as a diagnostic test for the evaluation of intestinal dysbiosis, irritable bowel syndrome, malabsorption, or small intestinal overgrowth of bacteria:
 - a. Triglycerides
 - b. Chymotrypsin
 - c. Iso-butyrate, iso-valerate, and n-valerate
 - d. Meat and vegetable fibers
 - e. Long chain fatty acids
 - f. Cholesterol
 - g. Total short chain fatty acids
 - h. Levels of Lactobacilli, bifidobacteria, and E. coli and other "potential pathogens," including Aeromona, Bacillus cereus, Campylobacter, Citrobacter, Klebsiella, Proteus, Pseudomonas, Salmonella, Shigella, S. aureus, Vibrio
 - i. Identification and quantitation of fecal yeast (including C. albicans, C. tropicalis, Rhodotorula and Geotrichum)
 - j. N-butyrate
 - k. Beta-glucuronidase
 - l. pH

- m. Short chain fatty acid distribution (adequate amount and proportions of the different short chain fatty acids reflect the basic status of intestinal metabolism)
- n. Fecal secretory IgA

Procedure Codes

Codes
82239, 82542, 82710, 82715, 82725, 82784, 83520, 83630, 83986, 84311, 87045, 87046, 87075, 87102, 87177, 87209, 87328, 87329, 87336, 87493, 87500, 87641, 87798, 89160

References:

Arasradnam, R. P., Brown, S., Forbes, A., Fox, M. R., Hungin, P., Kelman, L., . . . Walters, J. R. F. (2018). Guidelines for the investigation of chronic diarrhoea in adults: British Society of Gastroenterology, 3rd edition. *Gut*, 67(8), 1380. doi:10.1136/gutjnl-2017-315909

Bäckhed, F., The Wallenberg Laboratory, U. o. G., Sahlgrenska University Hospital, Göteborg, Sweden 41345, Institute for Genome Sciences at the University of Maryland School of Medicine, B., MD 21201, USA, Ringel, Y., Division of Gastroenterology and Hepatology, D. o. M., University of North Carolina at Chapel Hill, NC 27599, USA, Dairy & Food Culture Technologies, C., CO 80122, USA, . . . bfinlay@msl.ubc.ca. (2012). Defining a Healthy Human Gut Microbiome: Current Concepts, Future Directions, and Clinical Applications. *Cell Host & Microbe*, 12(5), 611-622. doi:10.1016/j.chom.2012.10.012

Bakken, J. S., Borody, T., Brandt, L. J., Brill, J. V., Demarco, D. C., Franzos, M. A., . . . Surawicz, C. (2011). Treating Clostridium Difficile Infection With Fecal Microbiota Transplantation. *Clinical Gastroenterology and Hepatology*, 9(12), 1044-1049. doi:10.1016/j.cgh.2011.08.014

Bernstein, C. N., Eliakim, A., Fedail, S., Fried, M., Gearry, R., Goh, K. L., . . . LeMair, A. (2016). World Gastroenterology Organisation Global Guidelines Inflammatory Bowel Disease: Update August 2015. *J Clin Gastroenterol*, 50(10), 803-818. doi:10.1097/mcg.0000000000000660

Berry, D., & Reinisch, W. (2013). Intestinal microbiota: a source of novel biomarkers in inflammatory bowel diseases? *Best Pract Res Clin Gastroenterol*, 27(1), 47-58. doi:10.1016/j.bpg.2013.03.005

BioHM. (2018). Retrieved from <https://biohmhealth.com/>

Carding, S., Verbeke, K., Vipond, D. T., Corfe, B. M., & Owen, L. J. (2015). Dysbiosis of the gut microbiota in disease. *Microb Ecol Health Dis*, 26. doi:10.3402/mehd.v26.26191

Casen, C., Vebo, H. C., Sekelja, M., Hegge, F. T., Karlsson, M. K., Ciemniejews ka, E., . . . Rudi, K. (2015). Deviations in human gut microbiota: a novel diagnostic test for determining dysbiosis in patients with IBS or IBD. *Aliment Pharmacol Ther*, 42(1), 71-83. doi:10.1111/apt.13236

Colombel, J. F., Shin, A., & Gibson, P. R. (2019). AGA Clinical Practice Update on Functional Gastrointestinal Symptoms in Patients With Inflammatory Bowel Disease: Expert Review. *Clin Gastroenterol Hepatol*, 17(3), 380-390.e381. doi:10.1016/j.cgh.2018.08.001



Costello, S. P., Hughes, P. A., Waters, O., Bryant, R. V., Vincent, A. D., Blatchford, P., . . . Andrews, J. M. (2019). Effect of Fecal Microbiota Transplantation on 8-Week Remission in Patients With Ulcerative Colitis: A Randomized Clinical Trial. *Jama*, 321(2), 156-164.
doi:10.1001/jama.2018.20046

Danilova, N. A., Abdulkhakov, S. R., Grigoryeva, T. V., Markelova, M. I., Vasilyev, I. Y., Boulygina, E. A., . . . Abdulkhakov, R. A. (2019). Markers of dysbiosis in patients with ulcerative colitis and Crohn's disease. *Ter Arkh*, 91(4), 17-24. doi:10.26442/00403660.2019.04.000211

Davidovics, Z. H., Michail, S., Nicholson, M. R., Kocolek, L. K., Pai, N., Hansen, R., . . . Kellermayer, R. (2019). Fecal Microbiota Transplantation for Recurrent Clostridium difficile Infection and Other Conditions in Children: A Joint Position Paper From the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition. *J Pediatr Gastroenterol Nutr*, 68(1), 130-143. doi:10.1097/mpg.0000000000002205

DNATestingChoice. (2019). Microbiome Testing. Retrieved from <https://dnatestingchoice.com/en-us/microbiome-testing>

Falony, G., Joossens, M., Vieira-Silva, S., Wang, J., Darzi, Y., Faust, K., . . . Raes, J. (2016). Population-level analysis of gut microbiome variation. *Science*, 352(6285), 560-564.
doi:10.1126/science.aad3503

FDA. (2019). Fecal Microbiota for Transplantation: Safety Communication- Risk of Serious Adverse Reactions Due to Transmission of Multi-Drug Resistant Organisms. Retrieved from <https://www.fda.gov/safety/medwatch-safety-alerts-human-medical-products/fecal-microbiota-transplantation-safety-communication-risk-serious-adverse-reactions-due>

FDA. (2020a). Fecal Microbiota for Transplantation: New Safety Information - Regarding Additional Protections for Screening Donors for COVID-19 and Exposure to SARS-CoV-2 and Testing for SARS-CoV-2. Retrieved from <https://www.fda.gov/safety/medical-product-safety-information/fecal-microbiota-transplantation-new-safety-information-regarding-additional-protections-screening>

FDA. (2020b). Fecal Microbiota for Transplantation: Safety Alert - Risk of Serious Adverse Events Likely Due to Transmission of Pathogenic Organisms. Retrieved from <https://www.fda.gov/safety/medical-product-safety-information/fecal-microbiota-transplantation-safety-alert-risk-serious-adverse-events-likely-due-transmission>

Frank, D. N., St Amand, A. L., Feldman, R. A., Boedeker, E. C., Harpaz, N., & Pace, N. R. (2007). Molecular-phylogenetic characterization of microbial community imbalances in human inflammatory bowel diseases. *Proc Natl Acad Sci U S A*, 104(34), 13780-13785.
doi:10.1073/pnas.0706625104

Genova. (2019). Organix® Dysbiosis Profile. Retrieved from <https://www.gdx.net/uk/product/organix-dysbiosis-test-urine>

Guarino, A., Ashkenazi, S., Gendrel, D., Lo Vecchio, A., Shamir, R., & Szajewska, H. (2014). European Society for Pediatric Gastroenterology, Hepatology, and Nutrition/European Society for Pediatric Infectious Diseases Evidence-Based Guidelines for the Management of Acute



Gastroenteritis in Children in Europe: Update 2014. 59(1), 132-152.
doi:10.1097/mpg.0000000000000375

Guinane, C. M., & Cotter, P. D. (2013). Role of the gut microbiota in health and chronic gastrointestinal disease: understanding a hidden metabolic organ. *Therap Adv Gastroenterol*, 6(4), 295-308. doi:10.1177/1756283x13482996

Holleran, G., Scaldaferri, F., Ianiro, G., Lopetuso, L., Mc Namara, D., Mele, M. C., . . . Cammarota, G. (2018). Fecal microbiota transplantation for the treatment of patients with ulcerative colitis and other gastrointestinal conditions beyond Clostridium difficile infection: an update. *Drugs Today (Barc)*, 54(2), 123-136. doi:10.1358/dot.2018.54.2.2760765

Hunt, R., Quigley, E., Abbas, Z., Eliakim, A., Emmanuel, A., Goh, K.-L., . . . Review, T. (2014). Coping With Common Gastrointestinal Symptoms in the Community: A Global Perspective on Heartburn, Constipation, Bloating, and Abdominal Pain/Discomfort May 2013. *J Clin Gastroenterol*, 48(7). Retrieved from https://journals.lww.com/jcge/Fulltext/2014/08000/Coping_With_Common_Gastrointestinal_Symptoms_in.4.aspx

IDSA/ACG/ASGE/AGA/NASPGHAN. (2013). Current Consensus Guidance on Donor Screening and Stool Testing for FMT. Retrieved from [https://www.naspghan.org/files/documents/Joint_Scty_Sign-on_FDA%20FMT_final%207.15.13%20\(1\).pdf](https://www.naspghan.org/files/documents/Joint_Scty_Sign-on_FDA%20FMT_final%207.15.13%20(1).pdf)

Johnston, R. (2021). An overview of the innate immune system. Retrieved from https://www.uptodate.com/contents/an-overview-of-the-innate-immune-system?search=dysbiosis&source=search_result&selectedTitle=1~20&usage_type=default&display_rank=1

Kau, A. L., Ahern, P. P., Griffin, N. W., Goodman, A. L., & Gordon, J. I. (2011). Human nutrition, the gut microbiome and the immune system. *Nature*, 474(7351), 327-336. doi:10.1038/nature10213

Kelly, C. R., Kahn, S., Kashyap, P., Laine, L., Rubin, D., Atreja, A., . . . Wu, G. (2015). Update on Fecal Microbiota Transplantation 2015: Indications, Methodologies, Mechanisms, and Outlook. *Gastroenterology*, 149(1), 223-237. doi:10.1053/j.gastro.2015.05.008

Kim, K. O., & Gluck, M. (2019). Fecal Microbiota Transplantation: An Update on Clinical Practice. *Clin Endosc*, 52(2), 137-143. doi:10.5946/ce.2019.009

Lacy, B. E., Pimentel, M., Brenner, D. M., Chey, W. D., Keefer, L. A., Long, M. D., & Moshiree, B. (2021). ACG Clinical Guideline: Management of Irritable Bowel Syndrome. *Am J Gastroenterol*, 116(1), 17-44. doi:10.14309/ajg.0000000000001036

Lamb, C. A., Kennedy, N. A., Raine, T., Hendy, P. A., Smith, P. J., Limdi, J. K., . . . Hawthorne, A. B. (2019). British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. *Gut*, 68(Suppl 3), s1. doi:10.1136/gutjnl-2019-318484

Ley, R. E., Peterson, D. A., & Gordon, J. I. (2006). Ecological and evolutionary forces shaping microbial diversity in the human intestine. *Cell*, 124(4), 837-848. doi:10.1016/j.cell.2006.02.017



- Ley, R. E., Turnbaugh, P. J., Klein, S., & Gordon, J. I. (2006). Microbial ecology: human gut microbes associated with obesity. *Nature*, 444(7122), 1022-1023. doi:10.1038/4441022a
- Lichtenstein, G. R., Loftus, E. V., Isaacs, K. L., Regueiro, M. D., Gerson, L. B., & Sands, B. E. (2018). ACG Clinical Guideline: Management of Crohn's Disease in Adults. Official journal of the American College of Gastroenterology | ACG, 113(4). Retrieved from https://journals.lww.com/ajg/Fulltext/2018/04000/ACG_Clinical_Guideline__Management_of_Crohn_s.10.aspx
- Lo Presti, A., Zorzi, F., Del Chierico, F., Altomare, A., Cocca, S., Avola, A., . . . Guarino, M. P. L. (2019). Fecal and Mucosal Microbiota Profiling in Irritable Bowel Syndrome and Inflammatory Bowel Disease. *Front Microbiol*, 10, 1655. doi:10.3389/fmicb.2019.01655
- Lozupone, C. A., Stombaugh, J. I., Gordon, J. I., Jansson, J. K., & Knight, R. (2012). Diversity, stability and resilience of the human gut microbiota. *Nature*, 489(7415), 220-230. doi:10.1038/nature11550
- Maaser, C., Sturm, A., Vavricka, S. R., Kucharzik, T., Fiorino, G., Annese, V., . . . Stoker, J. (2018). ECCO-ESGAR Guideline for Diagnostic Assessment in IBD Part 1: Initial diagnosis, monitoring of known IBD, detection of complications. *Journal of Crohn's and Colitis*, 13(2), 144-164K. doi:10.1093/ecco-jcc/jjy113
- Malham, M., Lilje, B., Houen, G., Winther, K., Andersen, P. S., & Jakobsen, C. (2019). The microbiome reflects diagnosis and predicts disease severity in paediatric onset inflammatory bowel disease. *Scand J Gastroenterol*, 1-7. doi:10.1080/00365521.2019.1644368
- Marietta, E., Mangalam, A. K., Taneja, V., & Murray, J. A. (2020). Intestinal Dysbiosis in, and Enteral Bacterial Therapies for, Systemic Autoimmune Diseases. *Front Immunol*, 11(2760). doi:10.3389/fimmu.2020.573079
- Michail, S., Nicholson, M., Kahn, S., & Kellermayer, R. (2020). Addendum for: Fecal Microbiota Transplantation for Recurrent Clostridium difficile Infection and Other Conditions in Children: A Joint Position Paper From the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition. *J Pediatr Gastroenterol Nutr*, 70(3). Retrieved from https://journals.lww.com/jpgn/Fulltext/2020/03000/Addendum_for__Fecal_Microbiota_Transplantation_for.27.aspx
- Mullish, B. H., Quraishi, M. N., Segal, J. P., McCune, V. L., Baxter, M., Marsden, G. L., . . . Williams, H. R. T. (2018). 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. *Gut*, 67(11), 1920. doi:10.1136/gutjnl-2018-316818
- Myneedu, K., Deoker, A., Schmulson, M. J., & Bashashati, M. (2019). Fecal microbiota transplantation in irritable bowel syndrome: A systematic review and meta-analysis. *United European Gastroenterol J*, 7(8), 1033-1041. doi:10.1177/2050640619866990
- NICE. (2017). Irritable bowel syndrome in adults: diagnosis and management. Retrieved from <https://www.nice.org.uk/guidance/cg61/chapter/1-Recommendations#diagnosis-of-ibs>



Pang, T., Leach, S. T., Katz, T., Day, A. S., & Ooi, C. Y. (2014). Fecal Biomarkers of Intestinal Health and Disease in Children. *Front Pediatr*, 2. doi:10.3389/fped.2014.00006

Parada Venegas, D., De la Fuente, M. K., Landskron, G., Gonzalez, M. J., Quera, R., Dijkstra, G., . . . Hermoso, M. A. (2019). Short Chain Fatty Acids (SCFAs)-Mediated Gut Epithelial and Immune Regulation and Its Relevance for Inflammatory Bowel Diseases. *Front Immunol*, 10, 277. doi:10.3389/fimmu.2019.00277

Pimentel, M., Saad, R. J., Long, M. D., & Rao, S. S. C. (2020). ACG Clinical Guideline: Small Intestinal Bacterial Overgrowth. *Official journal of the American College of Gastroenterology | ACG*, 115(2). Retrieved from https://journals.lww.com/ajg/Fulltext/2020/02000/ACG_Clinical_Guideline__Small_Intestinal_Bacterial.9.aspx

Qin, J., Li, R., Raes, J., Arumugam, M., Burgdorf, K. S., Manichanh, C., . . . Ehrlich, S. D. (2010). A human gut microbial gene catalogue established by metagenomic sequencing. *Nature*, 464(7285), 59-65. doi:10.1038/nature08821

Qin, J., Li, Y., Cai, Z., Li, S., Zhu, J., Zhang, F., . . . Kristiansen, K. (2012). A metagenome-wide association study of gut microbiota in type 2 diabetes. *Nature*, 490(7418), 55-60. doi:10.1038/nature11450

Raby, B. (2020). Tools for genetics and genomics: Polymerase chain reaction.

Rubin, D. T., Ananthakrishnan, A. N., Siegel, C. A., Sauer, B. G., & Long, M. D. (2019). ACG Clinical Guideline: Ulcerative Colitis in Adults. *Official journal of the American College of Gastroenterology | ACG*, 114(3). Retrieved from https://journals.lww.com/ajg/Fulltext/2019/03000/ACG_Clinical_Guideline__Ulcerative_Colitis_in.10.aspx

Saha, S., Mara, K., Pardi, D. S., & Khanna, S. (2021). Long-term Safety of Fecal Microbiota Transplantation for Recurrent Clostridioides difficile Infection. *Gastroenterology*, 160(6), 1961-1969.e1963. doi:10.1053/j.gastro.2021.01.010

Simren, M., Barbara, G., Flint, H. J., Spiegel, B. M., Spiller, R. C., Vanner, S., . . . Zoetendal, E. G. (2013). Intestinal microbiota in functional bowel disorders: a Rome foundation report. *Gut*, 62(1), 159-176. doi:10.1136/gutjnl-2012-302167

Snapper, S., & Abraham, C. (2020). Immune and microbial mechanisms in the pathogenesis of inflammatory bowel disease - UpToDate. Retrieved from https://www.uptodate.com/contents/immune-and-microbial-mechanisms-in-the-pathogenesis-of-inflammatory-bowel-disease?source=see_link

Vaughn, B. P., Rank, K. M., & Khoruts, A. (2018). Fecal Microbiota Transplantation: Current Status in Treatment of GI and Liver Disease. *Clin Gastroenterol Hepatol*. doi:10.1016/j.cgh.2018.07.026

Viome. (2019a, 03/28/2019). Demo Two. Retrieved from https://www.viome.com/storage/app/media/pdf/ViomeResults_BennySmalls.pdf



Viome. (2019b). Recommendations. Retrieved from
https://www.viome.com/storage/app/media/pdf/ViomeRecommendations_BennySmalls.pdf

Yu, E. W., Gao, L., Stastka, P., Cheney, M. C., Mahabamunuge, J., Torres Soto, M., ... Hohmann, E. L. (2020). Fecal microbiota transplantation for the improvement of metabolism in obesity: The FMT-TRIM double-blind placebo-controlled pilot trial. *PLoS Med*, 17(3), e1003051. doi:10.1371/journal.pmed.1003051

Zhang, H., DiBaise, J. K., Zuccolo, A., Kudrna, D., Braidotti, M., Yu, Y., ... Krajmalnik-Brown, R. (2009). Human gut microbiota in obesity and after gastric bypass. *Proc Natl Acad Sci U S A*, 106(7), 2365-2370. doi:10.1073/pnas.0812600106

Zhernakova, A., Kurilshikov, A., Bonder, M. J., Tigchelaar, E. F., Schirmer, M., Vatanen, T., ... Fu, J. (2016). Population-based metagenomics analysis reveals markers for gut microbiome composition and diversity. *Science*, 352(6285), 565-569. doi:10.1126/science.aad3369

Zoetendal, E. G., Akkermans, A. D., & De Vos, W. M. (1998). Temperature gradient gel electrophoresis analysis of 16S rRNA from human fecal samples reveals stable and host-specific communities of active bacteria. *Appl Environ Microbiol*, 64(10), 3854-3859. Retrieved from <http://dx.doi.org/>

Policy Update History:

5/1/2022	New policy
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