

(20426)

<b>Medical Benefit</b>		<b>Effective Date:</b> 01/01/13	<b>Next Review Date:</b> 07/21
<b>Preauthorization</b>	No	<b>Review Dates:</b> 09/12, 09/13, 07/14, 07/15, 07/16, 07/17, 07/18, 07/19, 07/20	

***This protocol considers this test or procedure investigational. If the physician feels this service is medically necessary, preauthorization is recommended.***

*The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.*

### RELATED PROTOCOLS

Fecal Calprotectin Testing

Fecal Microbiota Transplantation

Populations	Interventions	Comparators	Outcomes
Individuals: <ul style="list-style-type: none"> <li>With suspected intestinal dysbiosis, irritable bowel syndrome, malabsorption, or small intestinal bacterial overgrowth</li> </ul>	Interventions of interest are: <ul style="list-style-type: none"> <li>Fecal analysis testing</li> </ul>	Comparators of interest are: <ul style="list-style-type: none"> <li>Standard approach to diagnosing specific conditions</li> </ul>	Relevant outcomes include: <ul style="list-style-type: none"> <li>Test validity</li> <li>Symptoms</li> <li>Functional outcomes</li> </ul>

### DESCRIPTION

Intestinal dysbiosis may be defined as a state of disordered microbial ecology that is believed to cause disease. Laboratory analysis of fecal samples is proposed as a method of identifying individuals with intestinal dysbiosis and other gastrointestinal disorders.

### SUMMARY OF EVIDENCE

For individuals who have gastrointestinal conditions such as suspected intestinal dysbiosis, irritable bowel syndrome, malabsorption, or small intestinal bacterial overgrowth who receive fecal analysis testing, the evidence includes several cohort and case-control studies comparing fecal microbiota in patients who had a known disease with healthy controls. The relevant outcomes are test validity, symptoms, and functional outcomes. The available retrospective cohort studies on fecal analysis have suggested that some components of the fecal microbiome and inflammatory markers may differ across patients with irritable bowel syndrome subtypes. No studies were identified on the diagnostic accuracy of fecal analysis vs. another diagnostic approach or that compared health outcomes in patients managed with and without fecal analysis tests. No studies were identified that directly informed the use of fecal analysis in the evaluation of intestinal dysbiosis, malabsorption, or small

intestinal bacterial overgrowth. The evidence is insufficient to determine the effects of the technology on health outcomes.

## POLICY

Fecal analysis of the following components is considered **investigational** as a diagnostic test for the evaluation of intestinal dysbiosis, irritable bowel syndrome, malabsorption, or small intestinal overgrowth of bacteria:

- Triglycerides
- Chymotrypsin
- Iso-butyrate, iso-valerate, and *n*-valerate
- Meat and vegetable fibers
- Long-chain fatty acids
- Cholesterol
- Total short-chain fatty acids
- Levels of Lactobacilli, bifidobacteria, and Escherichia coli and other “potential pathogens,” including Aeromonas, Bacillus cereus, Campylobacter, Citrobacter, Klebsiella, Proteus, Pseudomonas, Salmonella, Shigella, Staphylococcus aureus, and Vibrio
- Identification and quantitation of fecal yeast (including Candida albicans, Candida tropicalis, Rhodotorula, and Geotrichum)
- *N*-butyrate
- $\beta$ -glucuronidase
- pH
- Short-chain fatty acid distribution (adequate amount and proportions of the different short-chain fatty acids reflect the basic status of intestinal metabolism)
- Fecal secretory immunoglobulin A.

## BACKGROUND

### FECAL MARKERS OF DYSBIOSIS

Laboratory analysis of both stool and urine has been investigated as markers of dysbiosis. Commercial laboratories may offer testing for comprehensive panels or individual components of various aspects of digestion, absorption, microbiology, and metabolic markers. Representative components of fecal dysbiosis testing are summarized in Table 1.

Table 1. Components of the Fecal Dysbiosis Marker Analysis

Markers	Analytes
Digestion	<ul style="list-style-type: none"> <li>• Triglycerides</li> <li>• Chymotrypsin</li> <li>• Iso-butyrate, iso-valerate, and <i>n</i>-valerate</li> <li>• Meat and vegetable fibers</li> </ul>
Absorption	<ul style="list-style-type: none"> <li>• Long-chain fatty acids</li> <li>• Cholesterol</li> </ul>

Markers	Analytes
	<ul style="list-style-type: none"> <li>Total fecal fat</li> <li>Total short-chain fatty acids</li> </ul>
Microbiology	<ul style="list-style-type: none"> <li>Levels of Lactobacilli, bifidobacteria, and <i>Escherichia coli</i> and other “potential pathogens,” including <i>Aeromonas</i>, <i>Bacillus cereus</i>, <i>Campylobacter</i>, <i>Citrobacter</i>, <i>Klebsiella</i>, <i>Proteus</i>, <i>Pseudomonas</i>, <i>Salmonella</i>, <i>Shigella</i>, <i>Staphylococcus aureus</i>, and <i>Vibrio</i></li> <li>Identification and quantitation of fecal yeast (including <i>Candida albicans</i>, <i>Candida tropicalis</i>, <i>Rhodotorula</i>, and <i>Geotrichum</i>) (optional viral and/or parasitology components)</li> </ul>
Metabolic	<ul style="list-style-type: none"> <li><i>N</i>-butyrate (considered key energy source for colonic epithelial cells)</li> <li><math>\beta</math>-glucuronidase</li> <li>pH</li> <li>Short-chain fatty acid distribution (adequate amount and proportions of the different short-chain fatty acids reflect the basic status of intestinal metabolism)</li> </ul>
Immunology	<ul style="list-style-type: none"> <li>Fecal secretory immunoglobulin A (as a measure of luminal immunologic function)</li> <li>Calprotectin</li> </ul>

Fecal calprotectin as a stand-alone test is addressed in the Fecal Calprotectin Testing Protocol.

A related topic, fecal microbiota transplantation, the infusion of intestinal microorganisms to restore normal intestinal flora, is addressed in the Fecal Microbiota Transplantation Protocol. Fecal microbiota transplantation has been rigorously studied for the treatment of patients with recurrent *Clostridium difficile* infection.

## REGULATORY STATUS

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of comprehensive testing for fecal dysbiosis.

---

Services that are the subject of a clinical trial do not meet our Technology Assessment and Medically Necessary Services Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment and Medically Necessary Services Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

## REFERENCES

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

- Emmanuel A, Landis D, Peucker M, et al. Faecal biomarker patterns in patients with symptoms of irritable bowel syndrome. *Frontline Gastroenterol*. Oct 2016;7(4):275-282. PMID 27761231
- Goepp J, Fowler E, McBride T, et al. Frequency of abnormal fecal biomarkers in irritable bowel syndrome. *Glob Adv Health Med*. May 2014;3(3):9-15. PMID 24891989

3. Andoh A, Kuzuoka H, Tsujikawa T, et al. Multicenter analysis of fecal microbiota profiles in Japanese patients with Crohn's disease. *J Gastroenterol*. Dec 2012;47(12):1298-1307. PMID 22576027
4. Sobhani I, Tap J, Roudot-Thoraval F, et al. Microbial dysbiosis in colorectal cancer (CRC) patients. *PLoS One*. Jan 27 2011;6(1):e16393. PMID 21297998
5. Joossens M, Huys G, Cnockaert M, et al. Dysbiosis of the faecal microbiota in patients with Crohn's disease and their unaffected relatives. *Gut*. May 2011;60(5):631-637. PMID 21209126
6. Langhorst J, Elsenbruch S, Koelzer J, et al. Noninvasive markers in the assessment of intestinal inflammation in inflammatory bowel diseases: performance of fecal lactoferrin, calprotectin, and PMN-elastase, CRP, and clinical indices. *Am J Gastroenterol*. Jan 2008;103(1):162-169. PMID 17916108
7. Genova Diagnostics. 2015; [www.gdx.net](http://www.gdx.net). Accessed November 7, 2019.