Medical Policy
Fecal Calprotectin Testing

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Policy Number: 329
BCBSA Reference Number: 2.04.69
NCD/LCD: NA

Related Policies
- Fecal Analysis in the Diagnosis of Intestinal Dysbiosis, #556

Policy
Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO BlueSM and Medicare PPO BlueSM Members

Fecal calprotectin testing is INVESTIGATIONAL in the diagnosis and management of intestinal conditions, including the diagnosis and management of inflammatory bowel disease.

Prior Authorization Information
Pre-service approval is required for all inpatient services for all products. See below for situations where prior authorization may be required or may not be required for outpatient services.
Yes indicates that prior authorization is required.
No indicates that prior authorization is not required.
N/A indicates that this service is primarily performed in an inpatient setting.

<table>
<thead>
<tr>
<th>Outpatient</th>
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<tr>
<td>Commercial Managed Care (HMO and POS)</td>
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<tr>
<td>Commercial PPO and Indemnity</td>
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<tr>
<td>Medicare HMO BlueSM</td>
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<td>Medicare PPO BlueSM</td>
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CPT Codes / HCPCS Codes / ICD Codes
Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.
Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

The following CPT code is considered investigational for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

CPT Codes

<table>
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<tr>
<th>CPT codes:</th>
<th>Code Description</th>
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<tbody>
<tr>
<td>83993</td>
<td>Calprotectin, fecal</td>
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Description

INFLAMMATORY BOWEL DISEASE

Inflammatory bowel disease (IBD) is a chronic condition that encompasses 2 main forms: Crohn disease and ulcerative colitis, which overlap in clinical and pathologic characteristics but have distinct features. Crohn disease can involve the entire gastrointestinal (GI) tract and is characterized by transmural inflammation. Ulcerative colitis involves inflammation limited to the mucosal layer of the colon, almost always involving the rectum.

IBD is suggested by the presence of 1 or more of a variety of signs and symptoms that can be GI (eg, abdominal pain, bloody diarrhea, perianal fistulae), systemic (eg, weight loss, fatigue, growth failure in children), or extraintestinal (eg, characteristic rashes, uveitis, arthritis) in nature. Patients may present with or develop a range of severity levels, including life-threatening illness. Treatments include oral and rectal salicylates, glucocorticoids, immunomodulators (eg, methotrexate), and multiple biologic therapies (eg, infliximab), depending on disease severity, which are recommended by the American Gastroenterological Association and other organizations. Making a diagnosis of IBD is associated with well-defined management changes.

Diagnostic Methods

A typical diagnostic approach to IBD includes stool testing for enteric pathogens, blood tests (complete blood count, inflammatory markers) to evaluate disease severity, as well as small bowel imaging and endoscopy (upper GI, colonoscopy) with biopsies.

Fecal Calprotectin

In some cases, the clinical manifestations of IBD can be nonspecific and suggestive of other disorders, including infectious colitis, colon cancer, and functional bowel disorders, including irritable bowel syndrome.

Therefore, there is need for simple, accurate, noninvasive tests to detect intestinal inflammation. Potential noninvasive markers of inflammation fall into several categories, including serologic and fecal. Serologic markers such as C-reactive protein and antineutrophil cytoplasmic antibodies tend to have low sensitivity and specificity for intestinal inflammation because they are affected by inflammation outside of the GI tract. Fecal markers, in contrast, have the potential for being more specific to the diagnosis of GI tract disorders, because their levels are not elevated in extra digestive processes. Fecal leukocyte testing has been used to evaluate whether there is intestinal mucosal inflammation. The level of fecal leukocytes can be determined by the microscopic examination of fecal specimens; however, leukocytes are unstable and must be evaluated promptly by skilled personnel. There is interest in identifying stable proteins in stool specimens, which may be representative of the presence of leukocytes, rather than evaluating leukocyte levels directly.

Fecal calprotectin is 1 protein that could be used as a marker of inflammation. It is a calcium- and zinc-binding protein that accounts for approximately 60% of the neutrophils' cytoplasmic proteins. It is released
from neutrophils during activation or apoptosis/necrosis and has a role in regulating inflammatory processes. In addition to potentially higher sensitivity and specificity than serologic markers, another advantage of fecal calprotectin as a marker is that it has been shown to be stable in feces at room temperature for up to 1 week, leaving enough time for patients to collect samples at home and send them to a laboratory for testing. In contrast, lactoferrin, also a potential fecal marker of intestinal inflammation, is stable at room temperature for about 2 days.

Among potential disadvantages of fecal calprotectin as a marker of inflammation are that fecal calprotectin levels increase after use of nonsteroidal anti-inflammatory drugs, that levels may change with age, and that bleeding (e.g., nasal, menstrual) may cause an elevated fecal calprotectin level. Moreover, there is uncertainty about the optimal cutoff to distinguish between IBD and noninflammatory disease.

Fecal calprotectin testing has been used to differentiate between organic and functional intestinal disease. Some consider fecal calprotectin to be a marker of neutrophilic intestinal inflammation rather than a marker of organic disease and believe its appropriate use is to distinguish between IBD and non-IBD. In practice, the test might be suitable for selecting patients with IBD symptoms for endoscopy (i.e., deciding which patients do not require endoscopy). Fecal calprotectin testing has also been proposed to evaluate the response to IBD treatment and for predicting relapse. If found to be sufficiently accurate, results of calprotectin testing could be used to change treatment, such as adjusting medication levels.

**Summary**

Fecal calprotectin is a calcium- and zinc-binding protein that is a potential marker of intestinal inflammation. Fecal calprotectin testing is proposed as a noninvasive test to diagnose inflammatory bowel disease (IBD). Other potential uses are to evaluate treatment response for patients with IBD and as a marker of relapse.

For individuals who have suspected IBD who receive fecal calprotectin testing, the evidence includes prospective and retrospective diagnostic accuracy studies and systematic reviews. Relevant outcomes are test accuracy and validity, symptoms, change in disease status, quality of life, hospitalizations, and medication use. There is a large body of evidence evaluating the diagnostic accuracy of fecal calprotectin in patients considered to have IBD, and for whom irritable bowel syndrome is a consideration. In general, these studies have indicated that the commercially available test has very high sensitivity for IBD. Studies have varied in the cutoff of fecal calprotectin used to indicate the presence of disease, but most have used a cutoff of 50 μg/g. However, there is relatively little data on the use of calprotectin in the general population and potential for spectrum effect; given the possibility of more widespread use in practice, additional clinical validity data in the target population would be indicated. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have diagnosed IBD who receive fecal calprotectin testing for treatment assessment, or disease activity assessment, or relapse prediction, the evidence includes prospective and retrospective diagnostic studies, meta-analyses, and 1 randomized controlled trial. Relevant outcomes are test accuracy and validity, symptoms, change in disease status, quality of life, hospitalizations, and medication use. The diagnostic accuracy for fecal calprotectin for these indications is uncertain, as are the patient management changes associated with specific calprotectin levels. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Policy History**

<table>
<thead>
<tr>
<th>Date</th>
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<td>12/2015</td>
<td>Added coding language.</td>
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<tr>
<td>8/2015</td>
<td>New references added from BCBSA National medical policy.</td>
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<tr>
<td>7/2014</td>
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<tr>
<td>5/2013</td>
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Information Pertaining to All Blue Cross Blue Shield Medical Policies
Click on any of the following terms to access the relevant information:
Medical Policy Terms of Use
Managed Care Guidelines
Indemnity/PPO Guidelines
Clinical Exception Process
Medical Technology Assessment Guidelines

References
5. van Rheenen PF, Van de Vijver E, Fidler V. Faecal calprotectin for screening of patients with suspected inflammatory bowel disease: diagnostic meta-analysis. BMJ. 2010;341:c3369. PMID 20634346