MASSACHUSETTS

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Medical Policy

Fecal Calprotectin Testing

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Policy Number: 329

BCBSA Reference Number: 2.04.69 (For Plan internal use only)

Related Policies

Fecal Analysis in the Diagnosis of Intestinal Dysbiosis #556

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO Blue[SM] and Medicare PPO Blue[SM] Members

Fecal calprotectin testing may be considered **MEDICALLY NECESSARY** for the evaluation of patients when the differential diagnosis is inflammatory bowel disease or noninflammatory bowel disease (including irritable bowel syndrome) for whom endoscopy with biopsy is being considered.

Fecal calprotectin testing is considered **INVESTIGATIONAL** in the management of bowel disease, including the management of active inflammatory bowel disease and surveillance for relapse of disease in remission.

Prior Authorization Information

Inpatient

- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

Outpatient

- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	Prior authorization is **not required**.
Commercial PPO and Indemnity	Prior authorization is **not required**.
Medicare HMO Blue[SM]	Prior authorization is **not required**.
Medicare PPO Blue[SM]	Prior authorization is **not required**.

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 above medical necessity criteria MUST be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

CPT Codes

CPT codes:	Code Description
83993	Calprotectin, fecal

The following ICD Diagnosis Codes are considered medically necessary when submitted with the CPT code above if medical necessity criteria are met:

ICD-10-CM Diagnosis Coding

ICD-10-CM diagnosis codes:	Code Description
K52.3	Indeterminate colitis
K59.00	Constipation, unspecified
K59.01	Slow transit constipation
K59.02	Outlet dysfunction constipation
K59.04	Chronic idiopathic constipation
K59.09	Other constipation
K59.1	Functional diarrhea
K90.9	Intestinal malabsorption, unspecified
R10.0	Acute abdomen
R10.10	Upper abdominal pain, unspecified
R10.11	Right upper quadrant pain
R10.12	Left upper quadrant pain
R10.30	Lower abdominal pain, unspecified
R10.31	Right lower quadrant pain
R10.32	Left lower quadrant pain
R10.33	Periumbilical pain
R10.84	Generalized abdominal pain
R63.4	Abnormal weight loss
R10.9	Unspecified abdominal pain
R11.0	Nausea
R11.2	Nausea with vomiting, unspecified
R14.0	Abdominal distension (gaseous)
R14.1	Gas pain
R14.3	Flatulence
R19.4	Change in bowel habit

R19.5	Other fecal abnormalities
R19.7	Diarrhea, unspecified
R19.8	Other specified symptoms and signs involving the digestive system and abdomen

Description

Inflammatory Bowel Disease

Inflammatory bowel disease (IBD) is a chronic condition that encompasses 2 main forms: Crohn disease and ulcerative colitis. These conditions 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 of symptoms in the disease course, including life-threatening illness.

Diagnosis

Diagnosing IBD is associated with well-defined management changes. A typical diagnostic approach to IBD includes stool testing for enteric pathogens, blood tests (complete blood count, inflammatory markers) to differentiate etiologies and 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 non-specific and suggestive of other disorders, including infectious colitis, colon cancer, and functional bowel disorders, including irritable bowel syndrome (IBS).

Thus, there is a 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 anti-neutrophil cytoplasmic antibodies tend to have low sensitivity and specificity for intestinal inflammation because they are affected by inflammation outside the GI tract. Fecal markers, in contrast, have the potential to be 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.

Calprotectin is a 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 neutrophil's 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 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, another 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 the use of nonsteroidal anti-inflammatory drugs, that levels may change with age, and that bleeding (eg, 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 (eg, inflammation) and functional (no visible problem in the GI tract like IBS) disease. Some consider fecal calprotectin to be a marker of neutrophilic intestinal inflammation rather than a marker of organic disease and believe it has utility to distinguish between IBD and non-IBD. In practice, the test might be suitable for selecting patients with IBD symptoms for endoscopy (ie, 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.

Treatment
Guideline-based treatments of IBD include oral and rectal salicylates, glucocorticoids, immunomodulators (eg, methotrexate), and multiple biologic therapies (eg, infliximab), depending on disease severity.

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

Summary of Evidence
For individuals who have a suspicion of IBD when endoscopy with biopsy is being considered who receive fecal calprotectin testing to select patients who can forgo endoscopy, the evidence includes prospective and retrospective diagnostic accuracy studies and systematic reviews. Relevant outcomes are test validity, symptoms, change in disease status, quality of life (QOL), hospitalizations, and medication use. Twenty-eight studies in a systematic review evaluated the diagnostic accuracy of fecal calprotectin in patients suspected of having IBD for whom noninflammatory bowel disease, such as IBS, remains a consideration. Studies varied in the fecal calprotectin protein level cutoff used to indicate the presence of disease, but most used a cutoff of 50 µg/g, which is the recommended lower bound. Studies have indicated that, at this threshold, the test has a sensitivity of 93% to 99% for IBD and a negative predictive value of 73% to 100% for intestinal inflammation. Out of 100 cases of suspected IBD, approximately 49 invasive tests would be avoided with 1 case missed. In another more recent meta-analysis involving 19 studies where the majority of studies again used the cutoff of 50 µg/g, investigators determined that out of 100 hypothetical patients, 18 non-disease patients would have a colonoscopy performed and 1 patient with IBD would not be referred for a colonoscopy. Additionally, it was determined that incorporating a fecal calprotectin test into the regular diagnostic work-up would reduce the need for colonoscopy by 66.7%. Therefore, fecal calprotectin can be used to inform a decision of whether to proceed with endoscopy. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have active IBD who receive fecal calprotectin testing to monitor disease activity, the evidence includes a systematic review and 2 randomized controlled trials (RCTs). Relevant outcomes are test validity, symptoms, change in disease status, QOL, hospitalizations, and medication use. A systematic review determined that a fecal calprotectin level of 50 µg/g was the optimum threshold for triaging patients for endoscopy when they have symptoms of active disease. RCTs are needed to determine whether guiding treatment based on fecal calprotectin levels can improve disease management. A 2017 RCT included fecal calprotectin as 1 of several indicators of inflammation to test the effect of tight control of IBD on health outcomes. The independent contribution of fecal calprotectin could not be determined from this study design. In another RCT, self-monitoring with a home-based fecal calprotectin test among patients with established IBD demonstrated an increase in the proportion of patients seeking medical treatment; compliance to home-based testing in this study was low (29%). The use of a home-based fecal calprotectin test that is not available in the US limits the applicability of this study. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have IBD in remission who receive fecal calprotectin testing to predict relapse, the evidence includes a systematic review and an RCT. Relevant outcomes are test validity, symptoms,

change in disease status, QOL, hospitalizations, and medication use. A systematic review of studies that monitored fecal calprotectin in patients in remission demonstrated that fecal calprotectin levels began to rise 2 to 3 months before clinical relapse; an ideal fecal calprotectin cutoff for monitoring purposes was not identified. One RCT found no significant difference in the rate of relapse in patients whose medication was modified based on fecal calprotectin or standard clinical indicators, however, this RCT had design and conduct limitations that affected the interpretation of its results. Additional high-quality RCTs are needed to determine whether adding fecal calprotectin to standard clinical practice improves the management of IBD patients in remission. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Policy History

Date	Action
2/2022	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
2/2021	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
1/2020	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
5/2019	Annual policy review. New medically necessary indications described. Fecal calprotectin testing is medically necessary when the differential diagnosis is inflammatory bowel disease or irritable bowel syndrome for whom endoscopy with biopsy is being considered. Clarified coding information. Effective 5/1/2019.
4/2018	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
6/2017	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
12/2015	Added coding language.
8/2015	Annual policy review. New references added.
7/2014	Annual policy review. New references added.
5/2013	Annual policy review. New references added.
11/2011-4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No changes to policy statements.
12/2011	New policy effective 12/2011 describing ongoing non-coverage.

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

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