MASSACHUSETTS

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Medical Policy

Fecal Calprotectin Testing

Table of Contents

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[1]

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 individuals 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 **MEDICALLY NECESSARY** in the management of bowel disease, including the management of active inflammatory bowel disease and surveillance for relapse of disease in remission.[1]

Fecal calprotectin testing for any other indication is considered **INVESTIGATIONAL**.

Home based fecal calprotectin testing is considered **INVESTIGATIONAL**.

Fecal calprotectin testing concurrent with lactoferrin testing is considered **NOT MEDICALLY NECESSARY**.

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
K50.00	Crohn's disease of small intestine without complications
K50.011	Crohn's disease of small intestine with rectal bleeding
K50.012	Crohn's disease of small intestine with intestinal obstruction
K50.013	Crohn's disease of small intestine with fistula
K50.014	Crohn's disease of small intestine with abscess
K50.018	Crohn's disease of small intestine with other complication
K50.019	Crohn's disease of small intestine with unspecified complications
K50.10	Crohn's disease of large intestine without complications
K50.111	Crohn's disease of large intestine with rectal bleeding
K50.112	Crohn's disease of large intestine with intestinal obstruction
K50.113	Crohn's disease of large intestine with fistula
K50.114	Crohn's disease of large intestine with abscess
K50.118	Crohn's disease of large intestine with other complication
K50.119	Crohn's disease of large intestine with unspecified complications
K50.80	Crohn's disease of both small and large intestine without complications
K50.811	Crohn's disease of both small and large intestine with rectal bleeding
K50.812	Crohn's disease of both small and large intestine with intestinal obstruction
K50.813	Crohn's disease of both small and large intestine with fistula
K50.814	Crohn's disease of both small and large intestine with abscess
K50.818	Crohn's disease of both small and large intestine with other complication
K50.819	Crohn's disease of both small and large intestine with unspecified complications
K50.90	Crohn's disease, unspecified, without complications

K50.911	Crohn's disease, unspecified, with rectal bleeding
K50.912	Crohn's disease, unspecified, with intestinal obstruction
K50.913	Crohn's disease, unspecified, with fistula
K50.914	Crohn's disease, unspecified, with abscess
K50.918	Crohn's disease, unspecified, with other complication
K50.919	Crohn's disease, unspecified, with unspecified complications
K51.00	Ulcerative (chronic) pancolitis without complications
K51.011	Ulcerative (chronic) pancolitis with rectal bleeding
K51.012	Ulcerative (chronic) pancolitis with intestinal obstruction
K51.013	Ulcerative (chronic) pancolitis with fistula
K51.014	Ulcerative (chronic) pancolitis with abscess
K51.018	Ulcerative (chronic) pancolitis with other complication
K51.019	Ulcerative (chronic) pancolitis with unspecified complications
K51.20	Ulcerative (chronic) proctitis without complications
K51.211	Ulcerative (chronic) proctitis with rectal bleeding
K51.212	Ulcerative (chronic) proctitis with intestinal obstruction
K51.213	Ulcerative (chronic) proctitis with fistula
K51.214	Ulcerative (chronic) proctitis with abscess
K51.218	Ulcerative (chronic) proctitis with other complication
K51.219	Ulcerative (chronic) proctitis with unspecified complications
K51.30	Ulcerative (chronic) rectosigmoiditis without complications
K51.311	Ulcerative (chronic) rectosigmoiditis with rectal bleeding
K51.312	Ulcerative (chronic) rectosigmoiditis with intestinal obstruction
K51.313	Ulcerative (chronic) rectosigmoiditis with fistula
K51.314	Ulcerative (chronic) rectosigmoiditis with abscess
K51.318	Ulcerative (chronic) rectosigmoiditis with other complication
K51.319	Ulcerative (chronic) rectosigmoiditis with unspecified complications
K51.50	Left sided colitis without complications
K51.511	Left sided colitis with rectal bleeding
K51.512	Left sided colitis with intestinal obstruction
K51.513	Left sided colitis with fistula
K51.514	Left sided colitis with abscess
K51.518	Left sided colitis with other complication
K51.519	Left sided colitis with unspecified complications
K51.80	Other ulcerative colitis without complications
K51.811	Other ulcerative colitis with rectal bleeding
K51.812	Other ulcerative colitis with intestinal obstruction
K51.813	Other ulcerative colitis with fistula
K51.814	Other ulcerative colitis with abscess
K51.818	Other ulcerative colitis with other complication
K51.819	Other ulcerative colitis with unspecified complications
K51.90	Ulcerative colitis, unspecified, without complications
K51.911	Ulcerative colitis, unspecified with rectal bleeding
K51.912	Ulcerative colitis, unspecified with intestinal obstruction
K51.913	Ulcerative colitis, unspecified with fistula
K51.914	Ulcerative colitis, unspecified with abscess
K51.918	Ulcerative colitis, unspecified with other complication
K51.919	Ulcerative colitis, unspecified with unspecified complications
K58.0	Irritable bowel syndrome with diarrhea
K58.1	Irritable bowel syndrome with constipation
K58.2	Mixed irritable bowel syndrome

K58.8	Other irritable bowel syndrome
K58.9	Irritable bowel syndrome without diarrhea
K59.1	Functional diarrhea
K59.9	Functional intestinal disorder, unspecified
K90.9	Intestinal malabsorption, unspecified
K92.81	Gastrointestinal mucositis (ulcerative)
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
R10.9	Unspecified abdominal pain
R11.0	Nausea
R11.2	Nausea with vomiting, unspecified
R19.4	Change in bowel habit
R19.5	Other fecal abnormalities
R19.7	Diarrhea, unspecified
R63.4	Abnormal weight loss

Description

Inflammatory Bowel Disease

Inflammatory bowel disease (IBD) is a chronic condition that encompasses 2 main forms: Crohn's disease and ulcerative colitis. These conditions overlap in clinical and pathologic characteristics but have distinct features. Crohn's 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.[1,] It is a calcium- and zinc-binding protein that accounts for approximately 30-60% 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. A sample of a few grams of stool is sufficient enough for testing. A 50 mg/g fecal calprotectin concentration in a stool sample is usually recommended as the cutoff for the normal concentration for adults and children older than 4 years. Moderate increases in fecal calprotectin levels, up to 100 mg/g, have been described for individuals older than 65 years. The concentration of fecal calprotectin is physiologically higher for neonates, infants, and young children, and thus fecal calprotectin concentrations in this population should be interpreted with caution.

Among potential disadvantages of fecal calprotectin as a marker of inflammation are that fecal calprotectin levels increase after the use of some medications (ie, nonsteroidal anti-inflammatory drugs; proton pump inhibitors), and that levels may change with other factors such as age, low fiber intake, and lack of exercise; other clinical situations associated with mucosal inflammation may also cause elevated fecal calprotectin levels such as gastrointestinal bleeding.[1,2,]

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. 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

Description
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 irritable bowel syndrome (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 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. Moreover, a recent review found that fecal calprotectin is the most sensitive noninvasive test in distinguishing IBD from non-IBD with a sensitivity of 99%. 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 and predict relapse the evidence includes a meta-analysis (Mao), observational studies (Rosenfeld), prospective cohort study (Abej) and cross-sectional study (Campbell). Relevant outcomes are test validity, symptoms, change in disease status, QOL, hospitalizations, and medication use. Abej et al. (2016) performed a single-center cross-sectional study on a cohort of 240 people with IBD to determine the utility of fecal calprotectin on the management of persons with IBD in clinical practice. The authors concluded that fecal calprotectin "is a useful marker of disease activity and a valuable tool in managing persons with IBD in clinical practice" (Abej et al., 2016). An observational study conducted by Rosenfeld et al. (2016) evaluated perspectives of gastroenterologists on the impact of fecal calprotectin testing in management of patients with IBD. A total of 279 surveys were returned. Results demonstrated a "change in management 51.3% of the time which included a significant reduction in the number of colonoscopies performed." (Rosenfeld et al., 2016). A meta-analysis of the predictive capacity of fecal calprotectin in IBD relapse was conducted by Mao et al. (2012). The authors analyzed a total of 682 IBD patients and found that "pooled sensitivity and specificity of FC to predict relapse of quiescent IBD was 78% (95% confidence interval [CI]: 72-83) and 73% (95% CI: 68-77), respectively." Conclusion was that "as a simple and noninvasive marker, fecal calprotectin is useful in predicting relapse in quiescent IBD patient." (Mao et al., 2012). The evidence is sufficient to determine that the technology results in an improvement in net health outcome.

Policy History

Date	Action
3/2024	Policy revised to include medically necessary indications for fecal calprotectin testing in the management of bowel disease, active inflammatory bowel disease and surveillance for relapse of disease in remission. Effective 3/1/2024.
1/2024	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
2/2023	Annual policy review. Minor editorial refinements to policy statements; intent unchanged.
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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Endnotes

[1] Based on expert opinion