

Corporate Medical Policy

Fecal Calprotectin Test

File Name: fecal_calprotectin_test
Origination: 8/2009
Last CAP Review: 10/2011
Last Review: 10/2011

Active policy, no longer scheduled for routine literature review.

Description of Procedure or Service

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 response to treatment for patients with IBD and as a marker of relapse.

Background

Inflammatory bowel disease (IBD) is a chronic inflammatory condition. There are two main forms of the disorder, Crohn's disease (CD) and ulcerative colitis (UC). Typical symptoms of episodes/exacerbations are diarrhea, defecation urgency, and sometimes rectal bleeding and abdominal pain.

Noninvasive diagnosis of inflammatory intestinal disease is difficult because the clinical manifestation of intestinal disorders and colon cancer are relatively non-specific. For example, a patient presenting with diarrhea or abdominal pain has a wide range of diagnostic possibilities. Endoscopy with histology is the gold standard method for diagnosing bowel inflammation. Limitations of this approach are that it is invasive, with an associated risk of adverse events, and not well-tolerated by some patients.

There is, thus, the need for simple, accurate, noninvasive tests to detect intestinal inflammation. Potential noninvasive markers of inflammation fall into several categories including serological and fecal. Serologic markers such as C-reactive protein and anti-neutrophilcytoplasmic antibodies (ANCA) tend to have low sensitivity and specificity for intestinal inflammation because they are affected by inflammation outside of the gastrointestinal tract. Fecal markers, in contrast, have the potential for being more specific to the diagnosis of gastrointestinal disorders since 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 one protein that could possibly be used as a marker of inflammation. It is a calcium- and zinc-binding protein that accounts for about 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, a potential advantage of fecal calprotectin as a marker is that it has been shown to be stable in feces at room temperature for up to a week--leaving enough time for patients to collect samples at home and send them to a distant laboratory for testing. In contrast, lactoferrin, another potential fecal marker of intestinal inflammation, is stable at room temperature for only about 2 days.

Potential disadvantages of fecal calprotectin as a marker of inflammation include that fecal calprotectin

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levels increase after use of non-steroidal anti-inflammatory drugs, that levels may change with age, and that bleeding (e.g., nasal or menstrual) may cause an elevated fecal calprotectin level. Moreover, there is uncertainty about the optimal cutoff to use to distinguish between inflammatory bowel disease and non-inflammatory disease.

Fecal calprotectin testing has been used to distinguish between organic and functional intestinal disease. Some authors consider fecal calprotectin to be a marker of neutrophilic intestinal inflammation rather than a marker of organic disease and believe the appropriate use of the marker is to use it to distinguish between inflammatory bowel disease and non-inflammatory bowel disease. 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 potentially be used to change treatment such as adjusting medication levels.

There is a commercially available ELISA test measuring fecal calprotectin levels, the PhiCal™ (Genova Diagnostics). Recent literature from Europe has also discussed a rapid test for fecal calprotectin that could be used in the home; rapid tests have not been FDA-approved for use in the United States.

Regulatory Status

In March 2006, the PhiCal™ (Genova Diagnostics) quantitative ELISA test for measuring concentrations of fecal calprotectin in fecal stool was cleared for marketing by the Food and Drug Administration (FDA) through the 510(k) process. This test is indicated to aid in the diagnosis of inflammatory bowel disease and to differentiate IBD from irritable bowel syndrome (IBS); it is intended to be used in conjunction with other diagnostic testing and clinical considerations.

Related policy: Fecal Analysis in the Diagnosis of Intestinal Dysbiosis

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Policy

Active policy, no longer scheduled for routine literature review.

Fecal calprotectin testing is considered investigational. BCBSNC does not provide coverage for investigational services or procedures.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Fecal Calprotectin Test is covered

Not applicable.

When Fecal Calprotectin Test is not covered

Testing for fecal calprotectin is considered **investigational** in the diagnosis and management of intestinal conditions, including the diagnosis and management of inflammatory bowel disease.

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Policy Guidelines

Studies have consisted primarily of case series, which show high fecal calprotectin levels in patients with active inflammatory disease. However, use of fecal calprotectin in lieu of a standard workup for inflammatory bowel disease has not been demonstrated. Researchers claim that this test could be used to avoid more invasive testing or even reduce the number of tests needed but there are no studies that demonstrate this hypothesis. Questions remain regarding the utility of the fecal calprotectin test in the management of patients with inflammatory bowel disease.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: 83993

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

Bremner A, Roked S, Robinson R, Phillips I, et al. Fecal calprotectin in children with chronic gastrointestinal symptoms. *Acta Paediatr.* 2005;94(12):1855-58.

Langhorst J, Elsenbruch S, Koelzer J, et al. Noninvasive markers in the assessment of intestinal inflammation in inflammatory bowel disease: performance of fecal lactoferrin, calprotectin, and PMN-elastase, CRP, and clinical indices. *Am J Gastroenterol.* 2008 Jan;103(1):162-9.

Scarpa M, D'Inca R, Basso D, et al. Fecal lactoferrin and calprotectin after ileocolonic resection for Crohn's disease. *Dis Colon Rectum.* 2007 Jun;50(6):861-9.

Schroder O, Naumann M, Shastri Y, et al. Prospective evaluation of faecal neutrophil-derived proteins in identifying intestinal inflammation: combination of parameters does not improve diagnostic accuracy of calprotectin. *Aliment Pharmacol Ther.* 2007 1;26(7):1035-1042.

Schoepfer AM, Trummler M, Seeholzer P, et al. Accuracy of four fecal assays in the diagnosis of colitis. *Dis Colon Rectum.* 2007B;50(10):1697-1706.

Specialty Matched Consultant reviews, 2/2009

Senior Medical Director review 7/2009

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.60, 4/14/2011

Policy Implementation/Update Information

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| 8/31/09 | New policy. Reviewed with Senior Medical Director 7/9/2009. "Testing for fecal calprotectin is considered investigational for all indications. BCBSNC does not cover investigational services." Notice given 8/31/09. Policy effective date 12/7/09. (btw) |
| 4/13/10 | Description section revised. (adn) |

Fecal Calprotectin Test

- 6/22/10 Policy Number(s) removed. (amw)
- 11/23/10 Medical Director review. No change to policy statement. Policy status changed to “Active policy, no longer scheduled for routine literature review.” (adn)
- 11/8/11 Description section revised. Policy statement unchanged. When Fecal Calprotectin is Not Covered section revised to read: “Testing for fecal calprotectin is considered investigational in the diagnosis and management of intestinal conditions, including the diagnosis and management of inflammatory bowel disease.” Specialty Matched Consultant Advisory Panel review 10/26/11. Policy accepted as written. (adn)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.