



**EFFECTIVE DATE:** 04|01|2020  
**POLICY LAST UPDATED:** 02|20|2020

## OVERVIEW

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.

## MEDICAL CRITERIA

Not applicable

## PRIOR AUTHORIZATION

Not applicable

## POLICY STATEMENT

### BlueCHiP for Medicare

Fecal calprotectin testing is 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 not covered in the management of inflammatory bowel disease, including the management of active inflammatory bowel disease and surveillance for relapse of disease in remission as the evidence is insufficient to determine the effects of the technology on health outcomes.

### Commercial Products

Fecal calprotectin testing is 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 not medically necessary in the management of inflammatory bowel disease, including the management of active inflammatory bowel disease and surveillance for relapse of disease in remission as the evidence is insufficient to determine the effects of the technology on health outcomes.

## COVERAGE

Benefits may vary between groups and contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage or Subscriber Agreement for applicable laboratory not medically necessary/not covered benefits/coverage.

## BACKGROUND

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.

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, 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, 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. Therefore, fecal calprotectin can be used to inform a decision of whether to proceed with endoscopy. Clinical input supported that the use of fecal calprotectin testing for individuals with suspected IBD provides a clinically meaningful improvement in net health outcome by providing clinically valid and clinically useful information to guide the clinical decision-making. Specifically, fecal calprotectin testing can inform the decision by using a positive fecal calprotectin result to refer for endoscopy with biopsy or to use a negative fecal calprotectin results to exclude inflammatory bowel disease and avoid endoscopy with biopsy with acceptably low tradeoffs in missed diagnoses of IBD in those who have false negative FCP results. Input further highlighted that the use of fecal calprotectin is particularly important in pediatric populations, where children may not be able to fully participate as medical historians and may have non-specific and/or atypical symptoms. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have active IBD who receive fecal calprotectin testing to monitor disease activity, the evidence includes prospective and retrospective diagnostic studies, systematic reviews, and a randomized controlled trial (RCT). Relevant outcomes are test validity, symptoms, change in disease status, quality of life, hospitalizations, and medication use. RCTs are needed to determine whether guiding treatment based on fecal calprotectin levels can improve disease management. A 2017 RCT included fecal calprotectin as one 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. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have IBD in remission who receive fecal calprotectin testing to predict relapse, the evidence includes prospective and retrospective diagnostic studies, systematic reviews, and an RCT. Relevant outcomes are test validity, symptoms, change in disease status, quality of life, hospitalizations, and medication use. 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. Further study in high-quality RCTs is 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 the effects of the technology on health outcomes.

## **CODING**

### **BlueCHiP for Medicare and Commercial Products**

The following HCPCS codes are considered medically necessary when filed with the ICD-10 diagnosis codes listed below.

**83993** Calprotectin, fecal

### **ICD-10 Diagnosis Codes that may support medical necessity:**

K50.00-K50.919

K51.00-K51.019

K51.50-K51.919

K52.3

R19.8

## RELATED POLICIES

Not applicable

## PUBLISHED

Provider Update, April 2020

Provider Update, June 2019

Provider Update, February 2019

Provider Update, June 2017

Provider Update, January 2017

## REFERENCES

1. Waugh N, Cummins E, Royle P, et al. Faecal calprotectin testing for differentiating amongst inflammatory and non-inflammatory bowel diseases: systematic review and economic evaluation. *Health Technol Assess.* Nov 2013;17(55):xv-xix, 1-211. PMID 24286461
2. Otten CM, Kok L, Witteman BJ, et al. Diagnostic performance of rapid tests for detection of fecal calprotectin and lactoferrin and their ability to discriminate inflammatory from irritable bowel syndrome. *Clin Chem Lab Med.* 2008;46(9):1275-1280. PMID 18597588
3. Schoepfer AM, Trummel M, Seeholzer P, et al. Discriminating IBD from IBS: comparison of the test performance of fecal markers, blood leukocytes, CRP, and IBD antibodies. *Inflamm Bowel Dis.* Jan 2008;14(1):32-39. PMID 17924558
4. Basumani P, Bardhan K, Eyre R, et al. Faecal calprotectin: Rotherham experience (unpublished slide presentation). BSG Away; 2012 June 28.
5. Li XG, Lu YM, Gu F, et al. [Fecal calprotectin in differential diagnosis of irritable bowel syndrome] [Chinese]. *Beijing Da Xue Xue Bao Yi Xue Ban.* Jun 18 2006;38(3):310-313. PMID 16778979
6. El-Badry A, Sedrak H, Rashed L. Faecal calprotectin in differentiating between functional and organic bowel diseases. *Arab J Gastroenterol.* May 23 2010;11(2):70-73.
7. Van de Vijver E, Schreuder AB, Cnossen WR, et al. Safely ruling out inflammatory bowel disease in children and teenagers without referral for endoscopy. *Arch Dis Child.* Dec 2012;97(12):1014-1018. PMID 23019289
8. Sidler MA, Leach ST, Day AS. Fecal S100A12 and fecal calprotectin as noninvasive markers for inflammatory bowel disease in children. *Inflamm Bowel Dis.* Mar 2008;14(3):359-366. PMID 18050298
9. Damms A, Bischoff SC. Validation and clinical significance of a new calprotectin rapid test for the diagnosis of gastrointestinal diseases. *Int J Colorectal Dis.* Oct 2008;23(10):985-992. PMID 18629518
10. Henderson P, Casey A, Lawrence SJ, et al. The diagnostic accuracy of fecal calprotectin during the investigation of suspected pediatric inflammatory bowel disease. *Am J Gastroenterol.* Jun 2012;107(6):941-949. PMID 22370604
11. Bonnin Tomas A, Vila Vidal M, Rosell Camps A. [Fecal calprotectin as a biomarker to distinguish between organic and functional gastrointestinal disease] [Spanish]. *Rev Esp Enferm Dig.* Dec 2007;99(12):689-693. PMID 18290691

12. Fagerberg UL, Loof L, Myrdal U, et al. Colorectal inflammation is well predicted by fecal calprotectin in children with gastrointestinal symptoms. *J Pediatr Gastroenterol Nutr.* Apr 2005;40(4):450-455. PMID 15795593
13. Jorgensen LG, Fredholm L, Hyltoft Petersen P, et al. How accurate are clinical activity indices for scoring of disease activity in inflammatory bowel disease (IBD)? *Clin Chem Lab Med.* May 2005;43(4):403-411. PMID 15899657
14. Mosli MH, Zou G, Garg SK, et al. C-reactive protein, fecal calprotectin, and stool lactoferrin for detection of endoscopic activity in symptomatic inflammatory bowel disease patients: a systematic review and meta-analysis. *Am J Gastroenterol.* Jun 2015;110(6):802-819; quiz 820. PMID 25964225
15. Colombel JF, Panaccione R, Bossuyt P, et al. Effect of tight control management on Crohn's disease (CALM): a multicentre, randomised, controlled phase 3 trial. *Lancet.* Dec 23 2018;390(10114):2779-2789. PMID 29096949
16. Heida A, Park KT, van Rheenen PF. Clinical utility of fecal calprotectin monitoring in asymptomatic patients with inflammatory bowel disease: a systematic review and practical guide. *Inflamm Bowel Dis.* Jun 2017;23(6):894-902. PMID 28511198
17. Lasson A, Ohman L, Stotzer PO, et al. Pharmacological intervention based on fecal calprotectin levels in patients with ulcerative colitis at high risk of a relapse: A prospective, randomized, controlled study. *United European Gastroenterol J.* Feb 2015;3(1):72-79. PMID 25653861
18. Lichtenstein GR, Loftus EV, Isaacs KL, et al. ACG Clinical Guideline: management of Crohn's disease in adults. *Am J Gastroenterol.* Apr 2018;113(4):481-517. PMID 29610508
19. National Institute for Health and Care Excellence (NICE). Faecal calprotectin diagnostic tests for inflammatory diseases of the bowel [DG11]. 2013; <https://www.nice.org.uk/guidance/DG11>. Accessed January 22, 2018.

[CLICK THE ENVELOPE ICON BELOW TO SUBMIT COMMENTS](#)

This medical policy is made available to you for informational purposes only. It is not a guarantee of payment or a substitute for your medical judgment in the treatment of your patients. Benefits and eligibility are determined by the member's subscriber agreement or member certificate and/or the employer agreement, and those documents will supersede the provisions of this medical policy. For information on member-specific benefits, call the provider call center. If you provide services to a member which are determined to not be medically necessary (or in some cases medically necessary services which are non-covered benefits), you may not charge the member for the services unless you have informed the member and they have agreed in writing in advance to continue with the treatment at their own expense. Please refer to your participation agreement(s) for the applicable provisions. This policy is current at the time of publication; however, medical practices, technology, and knowledge are constantly changing. BCBSRI reserves the right to review and revise this policy for any reason and at any time, with or without notice. Blue Cross & Blue Shield of Rhode Island is an independent licensee of the Blue Cross and Blue Shield Association.

