

## FEP 2.04.69 Fecal Calprotectin Testing

**Effective Date:** July 15, 2018

**Related Policies:** None

### Fecal Calprotectin Testing

#### Description

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.

#### FDA REGULATORY STATUS

In March 2006, the PhiCal® (Genova Diagnostics), an enzyme-linked immunosorbent assay test for measuring concentrations of fecal calprotectin in fecal stool, was cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. This test is indicated as an aid in the diagnosis of IBD and to differentiate IBD from irritable bowel syndrome, when used with other diagnostic testing and clinical considerations.

The PhiCal®, as modified by Quest Diagnostics, is classified as a laboratory-developed test. Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments. The modified PhiCal® is available under the auspices of the Clinical Laboratory Improvement Amendments. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing.

In 2014, CalPrest® (Eurospital SpA, Trieste, Italy) and, in 2016, CalPrest®NG (Eurospital SpA) were cleared for marketing by FDA through the 510(k) process. According to the FDA summary, CalPrest® “is identical” to the PhiCal™ test “in that they are manufactured by Eurospital S.p.A. Trieste, Italy. Compared with CalPrest®, the “differences in CalPrest® NG include the name of the test on the labels, detection antibody, the use of a Horse-radish peroxidase /TMB conjugate/substrate system, the provided Stop solution, the concentration of calibrators and controls in the kit and the dynamic range of the assay.”

FDA product code: NXO.

Rapid fecal calprotectin tests that can be used in the home or physician’s office are commercially available in Europe and Canada (eg, Calprosmart, Calpro AS, Norway; Quantum Blue Calprotectin®, Bühlmann Laboratories, Switzerland). Rapid tests have not been approved by the FDA for use in the United States.

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### POLICY STATEMENT

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

### BENEFIT APPLICATION

Screening (other than the preventive services listed in the brochure) is not covered. Please see Section 6 General exclusions.

Benefits are available for specialized diagnostic genetic testing when it is medically necessary to diagnose and/or manage a patient's existing medical condition. Benefits are not provided for genetic panels when some or all of the tests included in the panel are not covered, are experimental or investigational, or are not medically necessary.

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

### RATIONALE

#### Summary of Evidence

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 disease activity assessment or relapse prediction, the evidence includes prospective and retrospective diagnostic studies, meta-analyses, and a 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.

### SUPPLEMENTAL INFORMATION

#### Practice Guidelines and Position Statements

##### National Institute for Health and Care Excellence

In 2013 (one of the recommendations was updated in 2017), the National Institute for Health and Care Excellence published guidance on fecal calprotectin testing for inflammatory diseases of the bowel.<sup>17</sup> The guidance made the following recommendations:

“Faecal calprotectin testing is recommended as an option to support clinicians with the differential diagnosis of inflammatory bowel disease (IBD) or irritable bowel syndrome (IBS) in adults with recent onset lower gastrointestinal symptoms for whom specialist assessment is being considered, if ...

- cancer is not suspected, having considered the risk factors (for example, age)....

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“Faecal calprotectin testing is recommended as an option to support clinicians with the differential diagnosis of IBD or non-IBD (including IBS) in children with suspected IBD who have been referred for specialist assessment....”

### American Gastroenterological Association Institute

In 2014, the American Gastroenterological Association Institute published guidelines on the identification, assessment, and initial medical treatment in Crohn disease.<sup>18,19</sup> Fecal calprotectin is listed among other clinical lab tests to assess inflammatory status.

### U.S. Preventive Services Task Force Recommendations

Not applicable.

### Medicare National Coverage

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

### REFERENCES

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### POLICY HISTORY

Date	Action	Description
December 2012	New Policy	Fecal calprotectin testing is considered not medically necessary in the diagnosis and management of intestinal conditions, including the diagnosis and management of inflammatory bowel disease.
June 2013	Update Policy	Policy updated with new literature. No changes to policy statement. References updated.
June 2014	Update Policy	Policy updated with literature review. No change in policy statement. References 2, 5, 16 and 19 added; others renumbered or removed.
September 2015	Update Policy	Policy updated with literature review; references 2, 8, 15-16, and 21 added. No change in policy statement.
March 2017	Administrative Review	Policy reviewed with no policy statement changes.
June 2018	Update Policy	Policy updated with literature review through January 8, 2018; references 4, 9-10, 12, and 18-19 added; references 17-18 updated; some references removed. Policy statement unchanged except "not medically necessary" corrected to "investigational" due to FDA 510k status.

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