Reimbursement Policy

Laboratory Testing for the Diagnosis of Inflammatory Bowel Disease

POLICY DESCRIPTION | INDICATIONS AND/OR LIMITATIONS OF COVERAGE | APPLICABLE STATE AND FEDERAL REGULATIONS | APPLICABLE CPT/HCPCS PROCEDURE CODES | EVIDENCE-BASED SCIENTIFIC REFERENCES | REVISION HISTORY

I. Policy Description

major disorders: ulcerative colitis and Crohn's disease each with distinct pathologic and clinical characteristics.[1]

Ulcerative colitis (UC) is a chronic inflammatory condition characterized by relapsing and remitting episodes of inflammation limited to the mucosal layer of the colon[2] beginning at the rectum and may extend in a proximal and continuous fashion to involve other parts of the colon.[3]

Crohn's disease (CD) is characterized by patchy transmural inflammation (skip lesions) of the gastrointestinal tract resulting in sinus tracts, and ultimately microperforations and fistulae.[2] It may also lead to fibrosis, strictures and to obstructive clinical presentations that are not typically seen in ulcerative colitis.[4,5]

II. Indications and/or Limitations of Coverage

Application of coverage criteria is dependent upon an individual's benefit coverage at the time of the request. Specifications pertaining to Medicare and Medicaid can be found in the "Applicable State and Federal Regulations" section of this policy document.

1) Fecal calprotectin **or** fecal lactoferrin testing (see Note 1) **MEETS COVERAGE CRITERIA** for any of the following situations:
   a) For the differential diagnosis between non-inflammatory gastrointestinal disease (e.g., IBS) and inflammatory gastrointestinal disease (e.g., IBD).
   b) To monitor individuals with IBD (e.g., assess for response to therapy or relapse).

The following does not meet coverage criteria due to a lack of available published scientific literature confirming that the test(s) is/are required and beneficial for the diagnosis and treatment of an individual's illness.

2) For all other situations not described above, fecal calprotectin and fecal lactoferrin testing **DOES NOT MEET COVERAGE CRITERIA.**

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3) For the workup and monitoring of individuals with inflammatory bowel disease (IBD), the use of serologic markers (e.g., anti-neutrophil cytoplasmic antibody [ANCA]; perinuclear ANCA; anti-*Saccharomyces cerevisiae* antibody; antibody to Escherichia coli outer membrane porin C; anti-CBir1 flagellin antibody; antibody to *Pseudomonas fluorescens*-associated sequence I2; antichitobioside, antilaminaribioside, or antimannobioside antibodies; pyruvate kinase M2) **DOES NOT MEET COVERAGE CRITERIA**.

4) The use of multianalyte serum biomarker panels (with or without algorithmic analysis) that are designed to distinguish between IBD and non-IBD or that are designed to diagnose or monitor IBD (e.g. ibs-smart™, IBSchek®, PredictSURE IBD™ Test, Prometheus® testing) **DOES NOT MEET COVERAGE CRITERIA**.

NOTES:

Note 1: Fecal calprotectin is the preferred biomarker. If fecal calprotectin and fecal lactoferrin are ordered at the same time, only fecal calprotectin will be approved.

III. Applicable State and Federal Regulations

DISCLAIMER: If there is a conflict between this Policy and any relevant, applicable government policy for a particular member [e.g., Local Coverage Determinations (LCDs) or National Coverage Determinations (NCDs) for Medicare and/or state coverage for Medicaid], then the government policy will be used to make the determination. For the most up-to-date Medicare policies and coverage, please visit the Medicare search website: https://www.cms.gov/medicare-coverage-database/search.aspx. For the most up-to-date Medicaid policies and coverage, visit the applicable state Medicaid website.

Food and Drug Administration (FDA)

Many labs have developed specific tests that they must validate and perform in house. These laboratory-developed tests (LDTs) are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88). LDTs are not approved or cleared by the U. S. Food and Drug Administration; however, FDA clearance or approval is not currently required for clinical use.

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 U.S. Food and Drug Administration (FDA) through the 510(k) processes. This test is indicated to aid in the diagnosis of inflammatory bowel disease (IBD) and to differentiate IBD from irritable bowel syndrome (IBS); it is intended to be used in conjunction with other diagnostic testing and clinical

considerations.[101] On December 26, 2018, a successor device called "LIAISON Calprotectin, LIAISON Calprotectin Control Set, LIAISON Calprotectin Calibration Verifiers, LIAISON Q.S.E.T. Buffer, LIAISON Q.S.E.T. Device" was approved. The new description is as follows: "The DiaSorin LIAISON® Calprotectin assay is an in vitro diagnostic chemiluminescent immunoassay (CLIA) intended for the quantitative measurement, in human stool, of fecal calprotectin, a neutrophilic protein that is a marker of mucosal inflammation. The LIAISON® Calprotectin assay can be used as an aid in the diagnosis of inflammatory bowel diseases (IBD), specifically Crohn's disease and ulcerative colitis, and as an aid in differentiation of IBD from irritable bowel syndrome (IBS). Test results are to be used in conjunction with information obtained from the patients' clinical evaluation and other diagnostic procedures. The test has to be performed on the LIAISON® XL Analyzer."[102]

In January 2014, CalPrest® (Eurospital SpA, Trieste, Italy) was cleared for marketing by the FDA through the 510(k) processes. According to the FDA summary, CalPrest® "is identical" to the PhiCal™ test "in that they are manufactured by Eurospital S.p.A. Trieste, Italy. The only differences are the name of the test on the labels, the number of calibrators in the kit and the dynamic range of the assay." CalPrest®NG (Eurospital SpA) was cleared for marketing in November 2016.[103]

On October 16, 2018, the FDA approved the QUANTA Flash Calprotectin and Fecal Extraction Device. The device's intended use is as follows: "QUANTA Flash Calprotectin is a chemiluminescent immunoassay for the quantitative determination of fecal calprotectin in extracted human stool samples. Elevated levels of fecal calprotectin, in conjunction with clinical findings and other laboratory tests, can aid in the diagnosis of inflammatory bowel disease (IBD) (ulcerative colitis and Crohn's disease), and in the differentiation of IBD from irritable bowel syndrome (IBS)." This device has a predicate device, which was approved in 2017.[102]

On December 26, 2018, the FDA approved the LIAISON Calprotectin Assay. The device's intended use is as follows: "The DiaSorin LIAISON® Calprotectin assay is an in vitro diagnostic chemiluminescent immunoassay (CLIA) intended for the quantitative measurement, in human stool, of fecal calprotectin, a neutrophilic protein that is a marker of mucosal inflammation. The LIAISON® Calprotectin assay can be used as an aid in the diagnosis of inflammatory bowel diseases (IBD), specifically Crohn's disease and ulcerative colitis, and as an aid in differentiation of IBD from irritable bowel syndrome (IBS). Test results are to be used in conjunction with information obtained from the patients' clinical evaluation and other diagnostic procedures."[104]

On September 24, 2019, BUHLMANN Laboratories AG received FDA approval for the Buhlmann FCAL Turbo and CALEX Cap fecal calprotectin extraction device. This device is to be used in conjunction with the automated calprotectin test, BÜHLMANN fCAL® turbo. The BÜHLMANN fCAL® turbo is an in vitro diagnostic assay which quantitatively measures fecal calprotectin.[105]

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Rapid fecal calprotectin tests, such as CalproSmart™, are available internationally for use as point-of-care testing, but these have not been approved for use in the U.S. by the FDA.

IV. Applicable CPT/HCPCS Procedure Codes

CPT	Code Description
81401	Molecular pathology procedure, Level 2 (e.g., 2-10 SNPs, 1 methylated variant, or 1 somatic variant [typically using nonsequencing target variant analysis], or detection of a dynamic mutation disorder/triplet repeat)
81479	Unlisted molecular pathology procedure
82397	Chemiluminescent assay
83516	Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; qualitative or semiquantitative, multiple step method
83630	Lactoferrin, fecal; qualitative
83993	Calprotectin, fecal
86021	Antibody identification; leukocyte antibodies
86036	Antineutrophil cytoplasmic antibody (ANCA); screen, each antibody
86037	Antineutrophil cytoplasmic antibody (ANCA); titer, each antibody
86255	Fluorescent noninfectious agent antibody; screen, each antibody
86671	Antibody; fungus, not elsewhere specified
88346	Immunofluorescence, per specimen; initial single antibody stain procedure
88350	Immunofluorescence, per specimen; each additional single antibody stain procedure (List separately in addition to code for primary procedure)
0164U	Gastroenterology (irritable bowel syndrome [IBS]), immunoassay for anti-CdtB and anti-vinculin antibodies, utilizing plasma, algorithm for elevated or not elevated qualitative results Proprietary test: ibs-smart™ Lab/Manufacturer: Gemelli Biotech
0176U	Cytolethal distending toxin B (CdtB) and vinculin IgG antibodies by immunoassay (i.e., ELISA) Proprietary test: IBSchek® Lab/Manufacturer: Commonwealth Diagnostics International, Inc
0598U	Gastroenterology (irritable bowel syndrome), IgG antibodies to 18 food items by microarray-based immunoassay, whole blood or serum, report as elevated (positive) or normal (negative) antibody levels. Proprietary test: inFoods® IBS Test Lab/Manufacturer: Ethos Laboratories, Biomerica

Procedure codes appearing in Medical Policy documents are included only as a general reference tool for each policy. They may not be all-inclusive.

V. Evidence-based Scientific References

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VI. Revision History

Revision Date	Summary of Changes
09/04/2025	Reviewed and Updated: Updated background, guidelines, and evidence-based scientific references. Literature review necessitated the following changes in coverage criteria: Combined contents of G2061-Fecal Calprotectin Testing in Adults with this policy. Results in the addition of new CC1 and CC2: "1) Fecal calprotectin or fecal lactoferrin testing (see Note 1) MEETS COVERAGE CRITERIA for any of the following situations: a) For the differential diagnosis between non-inflammatory gastrointestinal disease (e.g., IBS) and inflammatory gastrointestinal disease (e.g., IBD). b) To monitor individuals with IBD (e.g., assess for response to therapy or relapse). 2) For all other situations not described above, fecal calprotectin and fecal lactoferrin testing DOES NOT MEET COVERAGE CRITERIA." Former CC2, now CC4, edited for clarity. Now reads: "5) The use of multianalyte serum biomarker panels (with or without algorithmic analysis) that are designed to distinguish between IBD and non-IBD or that are designed to diagnose or monitor IBD (e.g. ibs-smart™, IBSchek®, PredictSURE IBD™ Test, Prometheus® testing) DOES NOT MEET COVERAGE CRITERIA." New Note 1: "Note 1: Fecal calprotectin is the preferred biomarker. If fecal calprotectin and fecal lactoferrin are ordered at the same time, only fecal calprotectin will be approved." Added CPT code 83630, 83993; 0598U (effective date 10/1/2025)

Reimbursement Policy