MEDICAL POLICY

Medical Policy Title	**Serum Antibodies for the Diagnosis of Inflammatory Bowel Disease**
Policy Number	**2.02.19**
Current Effective Date	**November 19, 2026**
Next Review Date	**November 2027**

Our medical policies are guides to evaluate technologies or services for medical necessity. Criteria are established through the assessment of evidence based, peer-reviewed scientific literature, and national professional guidelines. Federal and state law(s), regulatory mandates and the member's subscriber contract language are considered first in the determination of a covered service.
(Link to Product Disclaimer)

POLICY STATEMENT(S)

I. Serologic testing of biomarkers (e.g.; Prometheus IBD sgi Diagnostic testing) is considered **not medically necessary** including, but not limited to:

- A. Anti-neutrophil cytoplasmic antibodies (ANCA) or anti-Saccharomyces cerevisiae (ASCA);
- B. Antibodies of outer membrane porin C of the bacteria Eschericia coli (anti-OmpC);
- C. Pseudomonas fluorescens-associated sequence I2 (anti-I2);
- D. Flagellin CBir1 (anti-cBir1);
- E. Antichitobioside antibodies (ACCA IgA);
- F. Antilaminaribioside antibodies (ALCA IgG);
- G. Antimannobioside antibodies (AMCA IgG);
- H. for **ALL** indications including, but not limited to:
  1. To diagnose and monitor patients with inflammatory bowel disease (IBD);
  2. To distinguish ulcerative colitis (UC) from Crohn's disease (CD).

RELATED POLICIES

Not Applicable

POLICY GUIDELINE(S)

Not Applicable

DESCRIPTION

Inflammatory bowel disease (IBD) is a chronic disease of the gastrointestinal tract that consists of two related diseases, ulcerative colitis (UC) and Crohn’s disease (CD). Although UC and CD are generally considered distinctive forms of IBD, their clinical presentations commonly overlap. Furthermore, for approximately 10-15% of patients with IBD, the distinction between UC and CD

cannot be made with certainty. These patients are given a diagnosis of indeterminate colitis (IC). A correct diagnosis of IBD, especially the differentiation between CD and UC is highly important in determining treatment and prognosis. The diagnostic work-up of patients with IBD is relatively complicated, and endoscopic exam and biopsy are currently crucial components of the diagnosis. Less invasive, accurate diagnostic tools to distinguish between UC, CD, and cases of indeterminate colitis are needed.

It has been proposed that serological markers for IBD can be utilized, both to differentiate UC from CD, and to define patient subgroups (e.g., location of the disease, such as proximal versus distal bowel involvement). Other potential uses include determination of disease severity, prediction of response to anti-tumor necrosis factor (TNF) therapy, and identification of the susceptibility to IBD among family members of an affected individual. Anti-neutrophil cytoplasmic antibodies (ANCA) and anti-Saccharomyces cerevisiae antibodies (ASCA) have been the most extensively studied serological markers for use in the diagnosis of IBD. ANCA are a group of antibodies, which are specific for granulocyte antigens. Anti-neutrophil cytoplasmic antibodies with perinuclear staining (pANCA) have been most commonly described in IBD and have been linked with UC. Other antibodies that have recently been associated with CD include anti-OmpC, anti-cBir1, Anti-I2, ACCA, ALCA, and AMCA. Increased amounts and levels of an antibody's response have been suggested to predict a more complicated course of disease. Large prospective studies are needed, to validate these findings.

Recent data suggest that the presence of serological biomarkers might represent a genetic susceptibility, because patients who have positive antibodies may carry mutations in the NOD2/CARD15 gene or in toll-like receptor genes. However, future studies of larger cohorts with well-defined clinical characteristics and patient populations are needed, to determine the validity of this relationship.

The PROMETHEUS IBD sgi Diagnostic aims to help identify IBD and differentiates between UC and CD. It may also assess a patient's risk for more aggressive disease. The test includes the proprietary and patented serologic markers anti-CBir1, Anti-OmpC and DNAse-sensitive pANCA process as well as, the markers ASCA IgA (ACCA) and IgG (ALCA and AMCA). The sgi Diagnostic test also includes the ATG16L, ECM1, mkX2-3, and STAT3 genetics and inflammation markers such as VEGF, ICAM-1, VACAM-1, CRP, and SAA. The Smart Diagnostic Algorithm technology produces an IBD score; results are reported as consistent with IBD (consistent with ulcerative colitis, consistent with CD, or inconclusive for ulcerative colitis vs. CD) or not consistent with IBD. The test is intended for use in patients with clinical suspicion of IBD.

SUPPORTIVE LITERATURE

A published study compared the predictive values of the Prometheus Inflammatory Bowel Disease (IBD) Serology 7 (IBD7) panel (Prometheus Laboratories, San Diego, CA) with the predictive values of routine blood tests in a population of children referred for initial evaluation of suspected IBD (Benor 2010). Medical records of pediatric patients referred for evaluation of IBD for whom IBD7 testing was performed at Prometheus Laboratories between January 2006 and November 2008 were reviewed. Patients underwent diagnosis by pediatric gastroenterologists on the basis of clinical, radiologic, endoscopic, and pathologic evaluations. A total of 394 records were identified and 90

records were excluded on the basis of age of >21 years, previous diagnosis of IBD, or unclear diagnosis. The prevalence of IBD in this cohort was 38%. The sensitivity, specificity, positive predictive value, negative predictive value, and kappa value for the serological panel were 67%, 76%, 63%, 79%, and 42%, respectively, compared with values for a combination of three (3) abnormal routine laboratory test results of 72%, 94%, 85%, 79%, and 47%. The antiflagellin antibody assay, the newest assay added to the panel, had sensitivity of 50% and specificity of 53%. Repeat serological testing failed to produce consistent results for four (4) of 10 patients. The authors concluded this study showed, the IBD7 panel has lower predictive values than routine laboratory tests in pediatric screening for IBD.

The use of serological markers for patients with IBD has not been shown to improve health outcomes by reducing the need for other tests nor has it been proven to increase the accuracy of diagnosis for these patients. Large-scale prospective studies are required, to ascertain the predictive value and cost-effectiveness of the use of these serology markers in the screening and monitoring of IBD patients.

PROFESSIONAL GUIDELINE(S)

The American College of Gastroenterology (ACG) published clinical guidelines for the management of Crohn's disease in adults (Lichtenstein 2025). They do not support serologic testing and state the following:

- "Routine use of serologic markers of IBD to establish the diagnosis of Crohn's disease is not indicated."
- "Because of the heterogeneous nature of IBD there has been extensive research directed toward finding immunologic markers that would assist in disease diagnosis. These studies have focused on antibodies to microbial antigens and autoantibodies. Antiglycan antibodies are more prevalent in CD than in UC but have a low sensitivity, making their use in diagnosis less helpful. Tests have been developed that use a combination of serologic, genetic, and inflammatory markers to try to improve diagnostic efficacy; however, this combination of markers has not improved serology measurements usefulness as a screening tool."

ACG published clinical guidelines for the management of ulcerative colitis in adults (Rubin 2025). They do not support serologic testing and state the following:

- "We recommend against serologic antibody testing to establish or rule out a diagnosis of UC (strong recommendation, very low quality of evidence)"
- "We recommend against serologic antibody testing to determine the prognosis of UC (strong recommendation, very low quality of evidence)."
- "Serologic markers such as perinuclear anti-neutrophil cytoplasmic antibodies (pANCA) may be found in up to 70%of patients with UC, and combination of negative anti-Saccharomyces cerevisiae (ASCA) antibodies with elevated pANCA levels have been proposed to facilitate establishing a diagnosis of UC. However, the pooled sensitivity of antibody testing for diagnosis of UC is low, and such markers are not used for establishing or ruling out a diagnosis of UC. While pANCA positivity has also been associated with treatment refractory UC, the

evidence supporting this is limited and there is currently no role for such testing to determine the likelihood of disease evolution and prognosis."

REGULATORY STATUS

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 (CLIA).

Laboratories that offer laboratory-developed tests must be licensed by CLIA for high-complexity testing. More information is available at: Clinical Laboratory Improvement Amendments (CLIA) | FDA [accessed 2026 Oct 28]

CODE(S)

- Codes may not be covered under all circumstances.
- Code list may not be all inclusive (AMA and CMS code updates may occur more frequently than policy updates).
- (E/I)=Experimental/Investigational
- (NMN)=Not medically necessary/appropriate

CPT Codes

Code	Description
There are no specific CPT codes.	Codes 81479, 82397, 83516 83520, 86140, 88346 or 88350 may be used for billing PROMETHEUS IBD sgi Diagnostic; however, these codes are not specific to PROMETHEUS IBD.

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HCPCS Codes

Code	Description
Not Applicable	

ICD10 Codes

Code	Description
K50.00-K50.919	Crohn's disease [regional enteritis] (code range)
K51.00-K51.919	Ulcerative colitis (code range)

REFERENCES

Benor S, et al. Shortcomings of the inflammatory bowel disease Serology 7 panel. Pediatrics. 2010 Jun;125(6):1230-6.

Lichtenstein GR, et al. ACG Clinical Guideline: management of Crohn's disease in adults. Am J Gastroenterol. 2025 Jun 3;120(6):1225-1264.

Rubin DT, et al. ACG Clinical Guideline Update: ulcerative colitis in adults. Am J Gastroenterol. 2025 Jun 3;120(6):1187-1224.

SEARCH TERMS

Not Applicable

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

Serological Diagnosis of Inflammatory Bowel Disease or Prometheus IBD is not addressed in National or Regional Medicare coverage determinations or policies.

PRODUCT DISCLAIMER

- Services are contract dependent; if a product does not cover a service, medical policy criteria do not apply.
- If a commercial product (including an Essential Plan or Child Health Plus product) covers a specific service, medical policy criteria apply to the benefit.
- If a Medicaid product covers a specific service, and there are no New York State Medicaid guidelines (eMedNY) criteria, medical policy criteria apply to the benefit.
- If a Medicare product (including Medicare HMO-Dual Special Needs Program (DSNP) product) covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit.
- If a Medicare HMO-Dual Special Needs Program (DSNP) product DOES NOT cover a specific service, please refer to the Medicaid Product coverage line.

POLICY HISTORY/REVISION

Committee Approval Dates

05/21/03, 04/15/04, 02/17/05, (Deleted 10/20/05-01/21/10), 01/21/10, 11/17/11, 12/20/12, 12/19/13, 11/20/14, 11/19/15, 11/17/16, 11/16/17, 12/20/18, 12/19/19, 12/17/20, 12/16/21, 11/17/22, 11/16/23, 11/21/24, 11/20/25, 11/19/26

Date	Summary of Changes
11/19/26	• Annual review, policy intent unchanged.

11/20/25	• Annual review, policy intent unchanged.
01/01/25	• Summary of changes tracking implemented.
05/21/03	• Original effective date