Effective November 1, 2023, refer to CMS Manual 100-02, Chapter 16-General Exclusions from Coverage for services included in this policy.

BlueCross BlueShield of Alabama

Name of Blue Advantage Policy:

Serum Antibodies for the Diagnosis of Inflammatory Bowel Disease

Policy #: 285
Latest Review Date: October 2022
Category: Laboratory
ARCHIVED EFFECTIVE 11/1/2023

BACKGROUND:

Blue Advantage *medical policy does not conflict with Local Coverage Determinations (LCDs), Local Medical Review Policies (LMRPs) or National Coverage Determinations (NCDs) or with coverage provisions in Medicare manuals, instructions or operational policy letters. In order to be covered by Blue Advantage the service shall be reasonable and necessary under Title XVIII of the Social Security Act, Section 1862(a)(1)(A). The service is considered reasonable and necessary if it is determined that the service is:*

1. *Safe and effective;*
2. *Not experimental or investigational*;*
3. *Appropriate, including duration and frequency that is considered appropriate for the service, in terms of whether it is:*

    - *Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;*
    - *Furnished in a setting appropriate to the patient's medical needs and condition;*
    - *Ordered and furnished by qualified personnel;*
    - *One that meets, but does not exceed, the patient's medical need; and*
    - *At least as beneficial as an existing and available medically appropriate alternative.*

Routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000 which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary by Medicare. Providers should bill* ***Original Medicare* *for covered services that are related to* ***clinical trials*** *that meet Medicare requirements (Refer to Medicare National Coverage Determinations Manual, Chapter 1, Section 310 and Medicare Claims Processing Manual Chapter 32, Sections 69.0-69.11).*

POLICY:

Blue Advantage will treat **the use of serologic markers** as a **non-covered benefit** and as **investigational** for all indications, including but not limited to:

- antibodies of outer membrane protein C of the bacteria Escherichia Coli (anti-OmpC of e. Coli)
- anti-chitobioside antibodies (ACCA IgA)
- anti-flagellin CBir1 (anti-CBir1)
- anti-laminaribioside antibodies (ALCA IgG)
- anti-mannobioside antibodies (AMCA IgG)
- anti-neutrophil cytoplasmic antibodies (ANCA)
- anti-saccharomyces cerevisiae (ASCA)
- Pseudomonas fluorescens Chrons disease-associated I2 sequence (P. fluorescens anti-I2)

Blue Advantage does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Advantage administers benefits based on the members' contract and medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

DESCRIPTION OF PROCEDURE OR SERVICE:

Inflammatory bowel disease (IBD) can be subdivided into ulcerative colitis (UC) and Crohn disease (CD), both of which present with symptoms of diarrhea and abdominal pain. Definitive diagnosis can usually be established by a combination of radiographic, endoscopic, and histologic criteria. In 10%–15% of cases, the distinction between ulcerative colitis and Crohn disease cannot be made with certainty.

Two serum antibodies, anti-neutrophilic cytoplasmic antibodies (ANCA) and anti-Saccharomyces cerevisiae (ASCA) may have several potential uses. They can be used as diagnostic tests to improve the efficiency and accuracy of diagnosing IBD to decrease the extent of the diagnostic workup or to avoid invasive tests. As a diagnostic test, they might also be useful in differentiating between UC and CD in cases of indeterminate colitis. A second potential use is to classify subtypes of IBD by location of disease (i.e., proximal versus distal bowel involvement) or by disease severity, thereby providing prognostic information. It has also been proposed that these markers may predict response to anti-tumor necrosis factor (TNF) therapy or identify susceptibility to IBD among family members of an affected individual.

The Prometheus© IBD Serology 7 (Prometheus Inc., San Diego, CA) is a quantitative analysis of biomarkers for IBD prediction and differentiation. Prometheus IBD Serology 7 is only offered at Prometheus. This system uses a two-step process to diagnose IBD and to differentiate between

UC and CD. The first step is a panel of four markers intended to maximize the sensitivity and negative predictive value of the test. Patients who test positive on the initial screen are further analyzed by a set of proprietary markers and enzyme reagents to distinguish between true positive results and artifacts of fixation. In this way, the Prometheus system is intended to increase the specificity of the test compared to other laboratories. The company also markets a testing strategy for predicting response to anti-TNF therapy and to monitor therapy.

KEY POINTS:

This policy is based evidence review most recently performed on October 20, 2023.

Summary of Evidence

Identified systematic reviews have identified regarding the use of Serum Antibodies for the Diagnosis of Inflammatory Bowel Disease technology. These reviews have found that the technology has relatively low sensitivities and is not completely specific to the inflammatory bowel disease. The clinical utility of this technology has not been demonstrated. No studies have been identified that demonstrate these serum markers could be used in lieu of the standard workup for IBD. No studies have been identified that demonstrate an actual decrease in the number of invasive tests performed because of the use serum markers. Further well-designed scientific studies are needed to evaluate the exact prognostic role of serologic markers which may help in the individual therapeutic management of pediatric and adult IBD. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Practice Guidelines and Position Statements

American College of Gastroenterology (ACG)

Institute for Clinical Systems Improvement (ICSI) Technology Assessment Committee

With regard to serum antibodies for diagnosing inflammatory bowel disease (IBD) the ICSI Technology Assessment Committee finds:

- The clinical utility of serological testing is not yet established for the diagnosis of inflammatory bowel disease in patients presenting with symptoms suggestive of IBD (Conclusion Grade III).
- The clinical utility of serological testing is not yet established for differentiating between UC and CD in patients with inflammatory bowel disease (Conclusion Grade II).
- Although serum testing is a safe procedure, there are risks associated with false negative and false positive test results. Consequences due to false negative and false positive test results have not been evaluated.
- There are well-established radiologic, histologic, and endoscopic techniques for diagnosing IBD and differentiating CD and UC.
- There appears to be a high inter-laboratory variability of sensitivities and specificities.

North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition / Crohn's and Colitis Foundation of America
In 2012, the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition stated that commercially available serologic assays mail fail to detect CD in at least 30% of children with this disorder and may wrongly suggest a diagnosis of IBD that is not supported by subsequent and definitive (endoscopic study) testing. They further stated that it may be most prudent for primary care providers to avoid ordering these tests and instead pursue referral and more conclusive specialty testing.

The North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the Crohn's and Colitis Foundation of America's consensus conference report on differentiating UC from CD in children and young adults stated that the clinical value of serology in patients with indeterminate colitis (IC) remains a topic of research, and further investigation should ascertain, among other areas, the role of surrogate laboratory markers (e.g., genetics, microbiology, and serology) in distinguishing these entities. A proposed algorithm to aid clinicians in differentiating UC from CD does not include serological testing.

U.S. Preventive Services Task Force
Not applicable.

KEY WORDS:
ANCA, Antibodies for the Diagnosis of Ulcerative Colitis and Crohn's Disease, ASCA, Crohn's Disease, (ANCA, ASCA), Prometheus System, Diagnosis of Inflammatory Bowel Disease, Ulcerative Colitis, Prometheus Labs, anti-neutrophil cytoplasmic antibody, anti-Saccharomyces cerevisiae antibody, DNA testing for Crohn's disease, inflammatory bowel disease, Prometheus, Prometheus Crohn's prognostic test for DNA testing, Prometheus NOD2/CARD15, Prometheus IBD sgi diagnostic, IBSchek, Biomarker, Serological antibody, antibodies of outer membrane porin C of the bacteria Eschericia coli, anti-OmpC, Pseudomonas fluorescens-associated sequence I2, anti-I2, flagellin CBir1, anti-cBir1, antichitobioside antibodies, ACCA IgA, antilaminaribioside antibodies, ALCA IgG, antimannobioside antibodies, AMCA IgG

APPROVED BY GOVERNING BODIES:
Serum testing for ANCA and ASCA is not U.S Food and Drug Administration (FDA) approved.

Analysis of anti-neutrophil cytoplasmic antibody (ANCA) and anti-Saccharomyces cerevisiae antibody (ASCA) may be performed in specific reference laboratories, (i.e., Prometheus© Inc.). Prometheus is located in San Diego, CA and licensed in several states including New York and California. It has not been cleared or approved by the U.S. Food and Drug Administration. Prometheus Laboratories Inc. is a CAP accredited CLIA laboratory.

BENEFIT APPLICATION:
Coverage is subject to member's specific benefits. Group-specific policy will supersede this policy when applicable.

CURRENT CODING:
CPT Codes:
There is no specific CPT code for detection of ANCA or ASCA. Providers may be using the following nonspecific CPT codes:

82397	Chemiluminescent assay
83516	Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; qualitative or semiquantitative, multiple step method
83520	Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; quantitative, not otherwise specified.
86140	C-reactive protein
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 (ibs-smart™)
0176U	Cytolethal distending toxin B (CdtB) and vinculin IgG antibodies by immunoassay (i.e., ELISA) (IBSSchek®)

PREVIOUS CODING:
CPT codes:

0085U	Cytolethal distending toxin B (CdtB) and vinculin IgG antibodies by immunoassay (i.e. ELISA) (Deleted 12/31/2020)

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POLICY HISTORY:

Adopted for Blue Advantage, July 2006
Available for comment August 22-October 5, 2006
Medical Policy Group, July 2008
Medical Policy Group, July 2010
Medical Policy Group, June 2012
Medical Policy Group, October 2015
Medical Policy Group, December 2015
Medical Policy Group, October 2019
Medical Policy Group, February 2020: Removed codes 81401 and 81479 from policy.
Medical Policy Group, March 2020: Quarterly coding update. Added new CPT code 0164U to Current Coding.
Medical Policy Group, August 2020: Quarterly coding update: Added CPT code 0176U to Current Coding for IBSchek.
Medical Policy Group, October 2020: 2021 Annual Coding Update. Code 0085U was already listed in Previous Coding Section. Added deleted effective date of 12/31/2020.
Medical Policy Group, December 2020
Medical Policy Group, December 2021
Medical Policy Group, October 2022
Medical Policy Group, October 2023: Reviewed by consensus. No new published peer-reviewed literature available that would alter the coverage statement in this policy.
Medical Policy Group, November 2023: Archived effective 11/1/2023.

providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield's administration of plan contracts.