



## Medical Policy

ARBenefits Approval: 10/12/11

Title: Serum Antibodies for  
Diagnosis of Inflammatory  
Bowel Disease

Effective Date: 01/01/2012

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Revision Date:

Code(s):

83516 Immunoassay for analyte other than infectious agent antibody or infectious agent antigen, qualitative or semiquantitative; multiple step method

86255 Fluorescent noninfectious agent antibody; screen, each antibody

88347 Immunofluorescent study, each antibody; indirect method

Administered by:  QualChoice®

## Public Statement:

Two serum antibodies, anti-neutrophilic cytoplasmic antibody (ANCA) and anti-Saccharomyces cerevisiae antibody (ASCA), have been investigated as a technique to improve the efficiency and accuracy of diagnosing Inflammatory Bowel Disease (IBD) in order to potentially decrease the extent of the diagnostic work-up or to avoid invasive diagnostic testing. Because of the low sensitivity and specificity, serum antibodies for diagnosis of inflammatory bowel disease are not covered.

## Medical Policy Statement:

Determination of anti-neutrophil cytoplasmic antibody (ANCA) and anti-saccharomyces cerevisiae antibody (ASCA) in the work-up and monitoring of patients with inflammatory bowel disease is considered investigational and is not covered

## Background:

Inflammatory bowed disease (IBD) can be subdivided into ulcerative colitis and Crohn's disease, both of which present with symptoms of diarrhea and abdominal pain. The definitive diagnosis can usually be established by a combination of radiographic, endoscopic and histologic criteria, although in 10-15% the distinction between the two

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cannot be made with certainty. Two serum antibodies, anti-neutrophilic cytoplasmic antibody (ANCA) and anti-Saccharomyces cerevisiae antibody (ASCA), have been investigated as a technique to improve the efficiency and accuracy of diagnosing IBD in order to potentially decrease the extent of the diagnostic work-up or to avoid invasive diagnostic testing. Testing of ANSA is available in most clinical laboratories, while ASCA is more recently described and may not be widely available.

The Prometheus System (Prometheus Inc.) is a commercially available diagnostic system that uses combinations of tests for ANCA and/or ASCA to aid in the diagnosis of IBD. This system initially uses an enzyme linked immunoadsorbent assay (ELISA) test to screen for ANCA or ASCA. Positive ANCA results are further analyzed by indirect immunofluorescence to determine the specific staining pattern. When a perinuclear pattern is obtained, specific enzyme reagents proprietary to the company are then used to distinguish between true positives and artifacts of fixation. In this way, the Prometheus system is intended to increase the specificity of the test compared to other laboratories. For ASCA, after a positive screen, the serum specimens are further analyzed by an ELISA microplate assay. Positive specimens are identified when the antibody level exceeds a predetermined cut-off point.

When ANCA and ASCA are used as a first screen in patients with clinical signs and symptoms suggestive of IBD, but who have not undergone confirmatory tests such as contrast radiographic studies or colonoscopy with biopsy, the average sensitivity is 38% with an average specificity of 94%. The low sensitivity indicates that a negative result will not be clinically helpful.

The average specificity of ANCA as a confirmatory test for ulcerative colitis and ASCA as a confirmatory test for Crohn's disease is 90% and 94% respectively. It is doubtful that this is high enough to confirm the diagnosis such that additional testing could be foregone.

In studies using ANCA and/or ASCA to distinguish between ulcerative colitis and Crohn's disease in patients who had already completed a conventional work-up the average specificity was 84%, still resulting in a significant number of patients being misclassified. There are no reported studies using these tests in a patient population with "indeterminate colitis".

Several studies evaluated the use of these markers for indications not covered in the original assessment. Several articles attempted to correlate titers of ANCA and/or ASCA with disease activity, but did not generally find such a correlation. Other studies evaluated the presence of serum markers in unaffected relatives of patients with IBD, reporting positive results in approximately 25%–50% of family members. However, these studies did not report on the incidence of IBD in these relatives with positive antibodies.

No studies demonstrated the use of these markers in lieu of a standard work-up for IBD. A number of authors claim that these markers can be used to avoid invasive testing, but

no studies demonstrated an actual decrease in the number of invasive tests through use of serum markers.

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## Application to Products

This policy applies to ARBenefits. Consult ARBenefits Summary Plan Description (SPD) for additional information.

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