

**Policy: MP218**

**Section: Medical Benefit Policy**

**Subject: Serum Antibodies and Gene Testing for the Diagnosis of Inflammatory Bowel Disease**

### Applicable Lines of Business

Commercial	X	CHIP	X
Medicare	X	ACA	X
Medicaid	X		

### I. Policy: Serum Antibodies and Gene Testing for the Diagnosis of Inflammatory Bowel Disease

#### II. Purpose/Objective:

To provide a policy of coverage regarding Serum Antibodies and Gene Testing for the Diagnosis of Inflammatory Bowel Disease

#### III. Responsibility:

- A. Medical Directors
- B. Medical Management

#### IV. Required Definitions

1. Attachment – a supporting document that is developed and maintained by the policy writer or department requiring/authoring the policy.
2. Exhibit – a supporting document developed and maintained in a department other than the department requiring/authoring the policy.
3. Devised – the date the policy was implemented.
4. Revised – the date of every revision to the policy, including typographical and grammatical changes.
5. Reviewed – the date documenting the annual review if the policy has no revisions necessary.

#### V. Additional Definitions

Medical Necessity or Medically Necessary means Covered Services rendered by a Health Care Provider that the Plan determines are:

- a. appropriate for the symptoms and diagnosis or treatment of the Member's condition, illness, disease or injury;
- b. provided for the diagnosis, and the direct care and treatment of the Member's condition, illness disease or injury;
- c. in accordance with current standards of good medical treatment practiced by the general medical community.
- d. not primarily for the convenience of the Member, or the Member's Health Care Provider; and
- e. the most appropriate source or level of service that can safely be provided to the Member. When applied to hospitalization, this further means that the Member requires acute care as an inpatient due to the nature of the services rendered or the Member's condition, and the Member cannot receive safe or adequate care as an outpatient.

#### Medicaid Business Segment

Medically Necessary — A service, item, procedure, or level of care that is necessary for the proper treatment or management of an illness, injury, or disability is one that:

- Will, or is reasonably expected to, prevent the onset of an illness, condition, injury or disability.
- Will, or is reasonably expected to, reduce or ameliorate the physical, mental or developmental effects of an illness, condition, injury or disability.
- Will assist the Member to achieve or maintain maximum functional capacity in performing daily activities, taking

into account both the functional capacity of the Member and those functional capacities that are appropriate for Members of the same age.

#### **DESCRIPTION:**

The Prometheus system is a commercially available diagnostic system that uses combinations of tests for anti-neutrophil cytoplasmic antibody (ANCA) and/or anti- *Saccharomyces cerevisiae* antibody (ASCA) to aid in the diagnosis of Inflammatory Bowel Disease (IBD). Tests/test panels include, but are not limited to the following:

#### Prometheus® IBD Serology 7

The American College of Gastroenterology states that serological studies are evolving to provide adjunctive support for the diagnosis of Crohn's disease but are not sufficiently sensitive or specific to be recommended for use as screening tools. Similarly, as reported in published ACG practice guidelines for ulcerative colitis, pANCA, and ASCA currently are not a definitive step in diagnosis or clinical decision making. pANCA detection alone is of little value in distinguishing between ulcerative colitis and Crohn's disease. The low sensitivity of pANCA for the diagnosis of ulcerative colitis prevents it from serving as a useful diagnostic tool.

The ACG also states that the measurement of genetic mutations of Crohn's disease has not been proven to be of clinical benefit for the diagnosis, management, or prediction of response to specific therapies.

#### **EXCLUSIONS:**

The Plan does not cover the use of anti-neutrophil cytoplasmic antibody (ANCA) and/or anti- *Saccharomyces cerevisiae* antibody (ASCA) ( e.g., Prometheus IBD Serology Testing) for the diagnosis of IBD because it is considered **unproven** and **NOT COVERED**. Although the specificity of these tests are relatively high (82-100%), the sensitivity is low (32 -50%), which indicates that a negative result will not be clinically helpful. There is insufficient evidence in the peer-reviewed published medical literature to establish the effectiveness of this test on health outcomes when compared to established tests or technologies.

The Plan does not cover the use of gene testing to establish the risk or diagnosis of inflammatory bowel disease (including but not limited to, Prometheus Crohn's Prognostic panel, NOD2/CARD15 genotyping, PredictSURE IBD Test™, etc.) because it is considered **unproven** and therefore **NOT COVERED**. There is insufficient evidence in the peer-reviewed published medical literature to establish the effectiveness of this test on health outcomes when compared to established tests or technologies.

#### **Medicaid Business Segment:**

Any requests for services that do not meet criteria set in the PARP may be evaluated on a case by case basis

**Note:** A complete description of the process by which a given technology or service is evaluated and determined to be experimental, investigational or unproven is outlined in **MP 15 - Experimental Investigational or Unproven Services or Treatment**.

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#### **CODING ASSOCIATED WITH:** Serum Antibodies for the Diagnosis of Inflammatory Bowel Disease

*The following codes are included below for informational purposes and may not be all inclusive. Inclusion of a procedure or device code(s) does not constitute or imply coverage nor does it imply or guarantee provider reimbursement. Coverage is determined by the member specific benefit plan document and any applicable laws regarding coverage of specific services. Please note that per Medicare coverage rules, only specific CPT/HCPCS Codes may be covered for the Medicare Business Segment. Please consult the CMS website at [www.cms.gov](http://www.cms.gov) or the local Medicare Administrative Carrier (MAC) for more information on Medicare coverage and coding requirements.*

- 81401 Molecular pathology procedure, Level 2 (eg, 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
- 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 (ie, ELISA) {*IBScheck*®}

0203U Autoimmune (inflammatory bowel disease), mRNA, gene expression profiling by quantitative RT-PCR, 17 genes (15 target and 2 reference genes), whole blood, reported as a continuous risk score and classification of inflammatory bowel disease aggressiveness {PredictSURE IBD™ Test}

Current Procedural Terminology (CPT®) © American Medical Association: Chicago, IL

**LINE OF BUSINESS:**

**Eligibility and contract specific benefits, limitations and/or exclusions will apply. Coverage statements found in the line of business specific benefit document will supersede this policy. For Medicare, applicable LCD's and NCD's will supercede this policy. For PA Medicaid Business segment, this policy applies as written.**

**REFERENCES:**

Sabery, Nasim, Bass, Dorsey. Use of Serologic Markers as a Screening Tool in Inflammatory Bowel Disease Compared With Elevated Erythrocyte Sedimentation Rate and Anemia Pediatrics 2007 119: e193-e199.

Desplat-Jego S, Johanet C, Escande A, Goetz J, Fabien N, Olsson N, et al. Update on Anti-Saccharomyces cerevisiae antibodies, anti-nuclear associated anti-neutrophil antibodies and antibodies to exocrine pancreas detected by indirect immunofluorescence as biomarkers in chronic inflammatory bowel diseases: results of a multicenter study. World J Gastroenterol. 2007 Apr 28;13(16):2312-8.

Winifred S. Hayes, Inc. Medical Technology Directory. (2013, April; last update search March 2017). Serological assays for the diagnosis and management of inflammatory bowel disease: Ulcerative colitis

Hayes, Inc. Medical Technology Directory. (2013, March; last update search January 2017). Serological assays for the diagnosis and management of inflammatory bowel disease: Crohn's Disease

Kornbluth A, Sachar DB; Practice Parameters Committee of the American College of Gastroenterology. Ulcerative colitis practice guidelines in adults (update): American College of Gastroenterology, Practice Parameters Committee. Am J Gastroenterol. 2004 Jul;99(7):1371-85.

Accessed August 12,2008. Available at URL address:

<http://www.gi.org/physicians/clinicalupdates.asp#guidelines>

Shaw M, Gebhard R, Loftus E, Pieper-Bigelow C. Institute for Clinical Systems Improvement Technology Assessment Report #65. Serum antibodies for the diagnosis of inflammatory bowel disease (IBD): pANCA for ulcerative colitis (UC) and ASCA for Crohn's Disease (CD). ICSI; 2002. Accessed August 12, 2008. Available at URL address:

<http://www.icsi.org/index>

Anand V, Russell AS, Tsuyuki R, Fedorak R. Perinuclear antineutrophil cytoplasmic autoantibodies and anti-Saccharomyces cerevisiae antibodies as serological markers are not specific in the identification of Crohn's disease and ulcerative colitis. Can J Gastroenterol. 2008 Jan;22(1):33-6.

ECRI Institute. Hotline Response [database online]. Plymouth Meeting (PA): ECRI Institute; 2008 Nov 12. Serologic markers for the diagnosis of inflammatory bowel disease. Available at URL address: <http://www.ecri.org>

Lichtenstein GR, Hanauer SB, Sandborn WJ, and the Practice Parameters Committee of the American College of Gastroenterology. Management of Crohn's disease in adults. Am J Gastroenterol. 2009 Feb;104(2):465-83. Epub 2009 Jan 6. Accessed May 10, 2010 Available at URL address:  
<http://www.gi.org/physicians/clinicalupdates.asp#guidelines>

Benor S, Russell GH, Silver M, Israel EJ, Yuan Q, Winter HS., Shortcomings of the inflammatory bowel disease Serology 7 panel. Pediatrics. 2010 Jun;125(6):1230-6.

Hayes, Inc. Hayes Genetic Testing Evaluation (Report). Lansdale, PA: Hayes, Inc.; IBD sgi Diagnostic™ Test (Prometheus Inc.). Mar. 2018

Hayes, Inc. Hayes Genetic Testing Evaluation (Report). Lansdale, PA: Hayes, Inc. Use of Anti-Infliximab Antibody Levels to Monitor Infliximab Treatment in Patients with Inflammatory Bowel Disease (IBD) Dec. 2017

Peppercorn MA. Clinical manifestations, diagnosis and prognosis of Crohn's disease in adults. Last reviewed December 2013. UpToDate Inc., Waltham, MA.

Kovacs M, Papp M, Lakatos PL, et al. Low mannose-binding lectin (MBL) is associated with paediatric inflammatory bowel diseases and ileal involvement in patients with Crohn disease. *J Crohns Colitis*. 2013;7(2):134-141

Bonneau J, et al. Systematic review: new serological markers (anti-glycan, anti-GP2, anti-GM-CSF-Ab) in the prediction of IBD patient outcomes. *Autoimmun Rev* 2015 Mar;14(3):231-45.

Fengming Y, et al. Biomarkers of inflammatory bowel disease. *Dis Markers* 2014;710915

Papp M, et al. Serological studies in inflammatory bowel disease: how important are they? *Curr Opin Gastroenterol* 2014 Jul;30(4):359-64.

Kaul A, et al. Serum anti-glycan antibody biomarkers for inflammatory bowel disease diagnosis and progression: a systematic review and meta-analysis. *Inflamm Bowel Dis* 2012 Oct;28(10):1872-84.

Smalley W., Falck-Ytter C., et al. AGA Clinical Practice Guidelines on the Laboratory Evaluation of Functional Diarrhea and Diarrhea-Predominant Irritable Bowel Syndrome in Adults (IBS-D) *Gastroenterology*, 2019;157(3):851-854

Wang Y, Miller M, et al. Identifying Crohn's disease signal from variome analysis. *Genome Medicine* 2019;11(59)

Lacy, B. E., Pimentel, M., Brenner, D. M., et al ACG Clinical Guideline: Management of Irritable Bowel Syndrome. Official journal of the American College of Gastroenterology | ACG, 2021;116(1), 17-44.

Gao, X., & Zhang, Y. Serological markers facilitate the diagnosis of Crohn's disease. *Postgraduate Medicine*, 2021;133(3), 286-290

Nakov, R., Snegarova, V., Dimitrova-Yurukova, D., Velikova, T. Biomarkers in Irritable Bowel Syndrome: Biological Rationale and Diagnostic Value. *Digestive Diseases* 2022; 40(1), 23-32

This policy will be revised as necessary and reviewed no less than annually.

**Devised:** 08/2008

**Revised:** 05/10 (keywords); 5/16 (re-title, update content), 5/17, 4/20 (exclusion clarification), 8/20 (add gene testing exclusion)

**Reviewed:** 5/11, 5/12, 5/13, 5/14; 5/15, 4/18, 4/19, 8/21, 8/22, 8/23, 8/24

**CMS UM Oversight Committee Approval:** 12/23; 11/8/24

Geisinger Health Plan may refer collectively to health care coverage sponsors Geisinger Health Plan, Geisinger Quality Options, Inc., and Geisinger Indemnity Insurance Company, unless otherwise noted. Geisinger Health Plan is part of Geisinger, an integrated health care delivery and coverage organization.

Coverage for experimental or investigational treatments, services and procedures is specifically excluded under the member's certificate with Geisinger Health Plan. Unproven services outside of an approved clinical trial are also specifically excluded under the member's certificate with Geisinger Health Plan. This policy does not expand coverage to services or items specifically excluded from coverage in the member's certificate with Geisinger Health Plan. Additional information can be found in MP015 Experimental, Investigational or Unproven Services.

Prior authorization and/or pre-certification requirements for services or items may apply. Pre-certification lists may be found in the member's contract specific benefit document. Prior authorization requirements can be found at <https://www.geisinger.org/health-plan/providers/ghp-clinical-policies>

Please be advised that the use of the logos, service marks or names of Geisinger Health Plan, Geisinger Quality Options, Inc. and Geisinger Indemnity Insurance Company on a marketing, press releases or any communication piece regarding the contents of this medical policy is strictly prohibited without the prior written consent of Geisinger Health Plan. Additionally, the above medical policy does not confer any endorsement by Geisinger Health Plan, Geisinger Quality Options, Inc. and Geisinger Indemnity Insurance Company regarding the medical service, medical device or medical lab test described under this medical policy.