Priority Health

MEDICAL POLICY No. 91583-R15

MARKERS FOR DIGESTIVE DISORDERS

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Date Of Origin: February 9, 2011

Status: Current

Summary of Changes

Addition:

- Crohn's Prognostic, IBD sgi Diagnostic, and PredictSure IDB are experimental and investigational.
- Medical necessity criteria for Helicobacter pylori testing.

I. POLICY/CRITERIA

A. Inflammatory digestive disorders

1. Measurements of serum concentration of infliximab (IFX) or adalimumab (ADA) or vedolizumab (VDZ) or ustekinumab (UST) for reactive therapeutic drug monitoring of members with active inflammatory bowel disease (IBD) treated with anti-tumor necrosis factor (TNF) agents are considered medically necessary.
2. Measurements of anti-drug antibody to infliximab or adalimumab or vedolizumab or ustekinumab are medically necessary to assess therapy response (i.e., dose escalation) when the biologic agent drug level is below the therapeutic range and limited to 1 test per 6 months. Routine or serial testing is not medically necessary due to insufficient evidence demonstrating improvement in clinical outcomes or management.
3. Thiopurine methyltransferase (TPMT) phenotype (analysis of enzyme activity) and genotype (identification of specific variants) testing for thiopurine drug response may be medically necessary according to EviCore guidelines.
4. 6-thioguanine nucleotide (6-TGN) and 6-methylmercaptopurine nucleotide (6-MMPN) measurements (e.g., PRO-PredictR 6MP / azathioprine, PRO-Predict Metabolites) are medically necessary to monitor compliance in those not responding to 6-MP or azathioprine and to assess suspected toxicity.
5. Fecal measurement of calprotectin is medically necessary for the management of inflammatory bowel diseases (e.g., Crohn's disease, ulcerative colitis). It is not medically necessary for other indications because its clinical utility has not been established.
6. The following genetic tests are medically necessary according to Evicore guidelines:

a. PredictSURE IBD

7. The following tests are experimental and investigational because their clinical utility has not been established.
    a. Crohn's disease peptide antibody testing
    b. Crohn's Prognostic
    c. ECM1 and Stat-3 testing for ulcerative colitis
    d. IBD sgi Diagnostic
    e. Measurement of serum mannose-binding lectin
    f. Myeloperoxidase antibody testing for inflammatory bowel disease,
    g. Proactive therapeutic drug monitoring to predict therapeutic response in the management of IBD or UC (e.g., PredictrPK IFX)
    h. Proteinase-3 antibody testing,
    i. Raman spectroscopy for inflammatory bowel disease.

B. Celiac Disease

1. Serological testing of IgA anti-human tissue transglutaminase (TTG) antibodies (TGA), and IgA anti-endomysial antibodies (EMA) are medically necessary for any of the following indications:
    a. As a preliminary diagnostic test for persons with symptoms suggestive of celiac disease; *or*
    b. To monitor response to a gluten-free diet; *or*
    c. To screen first-degree relatives of individuals with celiac disease; *or*
    d. To screen persons with type 1 diabetes for celiac disease.
2. IgG-TTG and IgG-EMA are medically necessary for persons with symptoms suggestive of celiac disease and a serum IgA deficiency.
3. Deamidated gliadin antibodies (DGP) testing is medically necessary if IgA deficiency is present.
4. Serological tests individually or as part of a panel (IgA-AGA, IgG-AGA, IgA-TTG, and IgA-EMAt) for celiac disease (i.e. PROMETHEUS® Celiac PLUS, PROMETHEUS® Celiac Serology) are experimental and investigational as an alternative to biopsy for assessing mucosal damage in individuals with celiac disease, and for all other indications.
5. Genetic testing for HLA-DQ2 and HLA-DQ8 haplotypes is medically necessary ONLY for members with symptoms suggestive of celiac disease and indeterminate serology results. Genetic testing as initial screening in symptomatic or in asymptomatic individuals is experimental and investigational (i.e., MyCeliacID, PROMETHEUS® Celiac Genetics)**.**
6. The following tests are experimental and investigational for the diagnosis of celiac disease: (not an all-inclusive list):
    a. D-xylose and/or lactulose absorption test
    b. Intestinal permeability tests
    c. Salivary tests
    d. Small-bowel follow-through (barium follow-through examination)
    e. Stool studies

C. Helicobacter pylori (H. pylori): Testing for active H. pylori infection is considered medically necessary when one or more of the following clinical indications are present.

1. For individuals 18 years of age and older:

   a. Dyspepsia without alarm features in patients <60 years of age.
   b. Documented history of peptic ulcer disease (gastric or duodenal).
   c. Gastric MALT lymphoma.
   d. History of endoscopic resection of early gastric cancer (EGC)
   e. Gastric intestinal metaplasia (GIM)
   f. Post-endoscopic resection of early gastric cancer.
   g. Long-term nonsteroidal anti-inflammatory drug (NSAID) use.
   h. Unexplained iron deficiency anemia.
   i. Idiopathic thrombocytopenic purpura (ITP).
   j. Confirmation of eradication following appropriate antimicrobial therapy (≥4 weeks after completion of therapy).
   k. Family history of gastric cancer
   l. First-generation immigrants from a high prevalence area

2. For individuals less than 18 years of age:

   a. Urea breath testing or stool antigen testing meets coverage criteria in the following situations:

      - Chronic ITP with suspected H. pylori infection
      - To measure the success of eradication of H. pylori infection (follow-up measurement at least 4 weeks post-treatment)

   b. A biopsy-based endoscopic histology test and either a rapid urease test or a culture with susceptibility testing to diagnose an H. pylori infection meets coverage criteria in the following situations:

      - Gastric or duodenal ulcers
      - Refractory iron deficiency anemia (when other causes have been ruled out)

D. Hydrogen and Methane Breath Tests

1. Hydrogen and methane breath testing are considered medically necessary for suspected lactose intolerance.
2. At-home hydrogen and methane breath testing are not medically necessary.
   i. Trio-Smart Breath Test is experimental and investigational.

II. DESCRIPTION

Inflammatory bowel disease (IBD) includes two major disorders: ulcerative colitis (UC) and Crohn disease (CD). UC affects the colon and is characterized by inflammation of the mucosal layer. CD is characterized by transmural inflammation and may involve any portion of luminal gastrointestinal tract, from the oral cavity to the perianal area.

Crohn's disease has an unknown etiology that may be influenced by genetic, immunologic, and environmental factors. The American College of Gastroenterology (AGA) Practice Guidelines for Management of Crohn's disease in adults (Lichtenstein et al., 2018) states that the diagnosis of Crohn's disease (CD) is based on a combination of clinical presentation and endoscopic, radiologic, histologic, and pathologic findings that demonstrate some degree of focal, asymmetric, and transmural granulomatous inflammation of the luminal GI tract. Laboratory testing is complementary in assessing disease severity and complications of disease. There is no single laboratory test that can make an unequivocal diagnosis of CD. The sequence of testing is dependent on presenting clinical features. Routine use of serologic markers of IBD to establish the diagnosis of Crohn's disease is not indicated.

Ulcerative colitis is a chronic immune-mediated inflammatory disease in which abnormal reactions of the immune system cause inflammation and ulcers on the inner lining of the large intestine (NIDDK, 2020). The American College of Gastroenterology Ulcerative Colitis Practice Guidelines in Adults (2019) states that serologic markers such as perinuclear antineutrophil cytoplasmic antibodies (pANCAs) may be found in up to 70% of patients with UC, and combination of negative anti–Saccharomyces cerevisiae antibodies with elevated pANCA levels has 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. Although 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.

The North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the Crohn's and Colitis Foundation of America consensus conference report on differentiating UC from CD in children and young adults (Bousvaros, et al., 2007) states that the value of serology in a patient with IC remains a topic of study, and further research should examine, among other areas, the role of surrogate laboratory markers (genetics, serology, microbiology) in distinguishing these entities. A proposed algorithm to assist clinicians in differentiating UC from CD does not include serological testing.

The American Gastroenterological Association Clinical Guidelines for Therapeutic Drug Monitoring in Inflammatory Bowel Disease (Feuerstein et al, 2017) suggests reactive therapeutic drug monitoring (TDM) to guide treatment

changes in adults with active IBD treated with anti-TNF agents. However, the AGA does not recommend the use of routine proactive therapeutic drug monitoring in adult patients with inactive IBD treated with anti-TNF agents. Defined as the assessment of drug concentrations and anti-drug antibodies, TDM, is an important tool for optimizing biologic therapy. Anti-drug antibody testing in patients who are undergoing treatment for IBD has been proposed to help determine whether ongoing treatment is safe and effective and whether changes are needed. Many patients who initially benefit from treatment experience a gradual decline or loss of treatment efficacy, which is often attributable to formation of anti-drug antibody that inactivate or accelerate the clearance of the drugs from the bloodstream. Anti-drug antibody levels are usually measured with an enzyme-linked immunosorbent assay (ELISA), but in patients who are undergoing treatment with ADA, IFX, UST, VDZ, detecting ATI with a conventional ELISA is often not possible because of interference by the drugs in the blood sample. This interference can be overcome, but it requires specialized sample processing or a more complex assay technique. Prometheus Anser tests (Anser ADA, IFX, UST, and VDZ) are novel laboratory-developed tests that measure both serum drug and anti-drug antibodies. An Expert Consensus Development Meeting consisting of members of the BRIDGe group and TDM specialists reached consensus statements on the application of TDM in clinical practice (Papamichael, 2019) including when it would be appropriate to order drug/antibody concentration testing.

Celiac disease is an autoimmune disease of the small intestine caused by sensitivity to dietary gluten and related proteins that occurs in genetically predisposed people. Celica disease has a wide spectrum of clinical manifestations that resemble a multisystemic disorder rather than an isolated intestinal disease and is characterized by small bowel injury and the presence of specific antibodies (Rubio-Tapia, 2023). In patients with celiac disease, immune responses to gliadin fractions promote an inflammatory reaction, characterized by infiltration of the lamina propria and the epithelium with chronic inflammatory cells and villous atrophy. Serologic evaluation of tissue transglutaminase (tTG)- immunoglobulin A (IgA) antibody is the preferred test for detection of celiac disease in adults. Serologic testing of serum tissue transglutaminase (tTG)-immunoglobulin A (IgA) and endomysial (EMA)-IgA antibody tests have high sensitivities. Intestinal biopsy is required in most patients to confirm the diagnosis.

According to the American College of Gastroenterology Guidelines Update: Diagnosis and Management of Celiac Disease (2023), genetic testing for CD-compatible human leukocyte antigen (HLA) haplotype is not required for diagnosis in all cases but may be helpful in selected situations such as in the context of serology-histology discrepancy In a change from their previous guidelines, ACG no longer recommends the use of AGA antibodies to test for celiac disease (Rubio-Tapia, 2023). Assays for deamidated gliadin peptide (DGP) antibodies have been shown to have reasonably high accuracy. The use of anti-reticulin antibodies (ARA) in the diagnosis of celiac disease has fallen out of

favor. While IgA antibodies to reticulin connective tissue did see some use, primarily in pediatric celiac disease evaluation, and appeared to have test performance equal to or better than AGA, ARA was largely supplanted first by AGA for technical reasons and later on by EMA and tTG which had markedly better test performance (Adriaanse et al, 2015). In a review of literature and recommendations for serologic evaluation for celiac disease by Nandiwata and colleagues (2013), it was concluded that ARA assays lack optimal sensitivities and specificities for routine diagnostic use.

The USPSTF (2017) found inadequate evidence regarding the accuracy of screening tests for celiac disease in asymptomatic populations. The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for celiac disease in asymptomatic persons. Evidence is lacking, and the balance of benefits and harms cannot be determined.

Hydrogen/Methane Breath Testing

Hydrogen and methane breath testing is a non-invasive, accurate, standard method of diagnosing lactose intolerance. Lactose intolerance has a high prevalence worldwide, ranging between 57% and 65%. It is caused by a reduction or loss of the activity of the intestinal enzyme lactase−phlorizin hydrolase, responsible for the digestion of lactose. This alteration determines an increased osmotic load in the small intestine and the fermentation of lactose by the bacterial flora, which leads to a high production of short-chain fatty acids and gas. This is followed by the onset of abdominal pain, diarrhea, and flatulence. The diagnosis is essential to undertake an adequate treatment and, for this purpose, different methods have been tested. These include genetic test, hydrogen breath test (HBT), quick lactase test, and lactose tolerance test. HBT is the most used method because it is non-invasive, inexpensive, and highly sensitive and specific, as well as easy to perform. (Catanzaro et al., 2021). According to the American Society for Clinical Laboratory Science (ASCLS), hydrogen breath testing(H_2) is traditionally performed in an outpatient laboratory setting. A meta-analysis by Marton, Xue, and Szilagyi (2012) comparing the diagnostic accuracy of lactose H_2 breath tests found an overall sensitivity of 0.88 (CI 0.85–0.90) and specificity of 0.85 (CI 0.82–0.87). Home hydrogen breath testing has not been proven to be a reliable diagnostic method in current peer-reviewed, published literature.

American College of Gastroenterology Clinical Guideline: Small Intestinal Bacterial Overgrowth (2020) suggest the use of breath testing (glucose hydrogen or lactulose hydrogen) for the diagnosis of SIBO in patients with IBS (conditional recommendation, very low level of evidence),glucose hydrogen or lactulose hydrogen breath testing for the diagnosis of SIBO in symptomatic patients with suspected motility disorders" (conditional recommendation, very low level of evidence) and testing for SIBO using glucose hydrogen or lactulose hydrogen breath testing in symptomatic patients (abdominal pain, gas, bloating, and/or

diarrhea) with previous luminal abdominal surgery" (conditional recommendation, very low level of evidence).

Hydrogen and Methane-Based Breath Testing in Gastrointestinal Disorders: The North American Consensus (2017) suggest breath testing in the diagnosis of small intestinal bacterial overgrowth (moderate quality evidence) and to evaluate for excessive methane excretion on breath test in association with clinical constipation and slowing of gastrointestinal transit" (moderate quality evidence).

IBD sgi Diagnostic is a commercial proprietary assay combines serologic, genetic, and inflammatory biomarkers in a testing algorithm as an aid in differentiating IBD from IBS, and ulcerative colitis from Crohn's disease. The test includes 9 serological markers including antiFla-X, anti-A4-Fla2, anti-CBir1, anti-OMPC, and DNAse-sensitive pANCA, genetic evaluation of ATG16L1, STAT3, NKX2-3, and ECM1. Inflammatory markers include VEGF, ICAM, VCAM, CRP, and SAA.

Crohn's Prognostic is a commercial proprietary assay combines serologic testing (anti-CBir1, anti-OMPC, DNAse sensitive pANCA) and genetic markers (NOD2 variants SNPs 8,12,13) and employs an algorithm to quantify the probability of disease complications over time.

The PredictSURE IBD test is a reverse-transcriptase quantitative polymerase chain reaction performed on whole blood of untreated IBD patients, evaluating expression of 15 informative genes and 2 reference genes. The CD8 T cell gene expression signature generated is analyzed by a proprietary algorithm, which aims to predict which IBD patients will have a more aggressive disease course.

H. Pylori Testing

Since the discovery of *Helicobacter pylori* (*H. pylori*) in 1983, numerous detection methods for the presence of the bacterium have been developed. Each one of them has been associated with advantages and disadvantages. Noninvasive tests such as serology, urea breath test (UBT) and stool antigen tests are usually preferred by clinicians. Serology has its own limitations, especially in endemic areas while UBT is technically very demanding. The stool antigen detection method, although specific, is usually associated with poor sensitivity. The UBT is believed to be specific, however the stomach is colonized by many other urease producing bacteria, which makes it questionable. Histology, culture, rapid urease test and polymerase chain reaction (PCR) are the tests which are carried out on antral biopsies collected by invasive means. Histology has been proposed to be very sensitive and specific, but doubts have been raised about how examining the morphology of the bacteria in the microscope can yield the conclusion that the bacterium is exclusively *H. pylori*. Rapid urease test (RUT) is also challenged because the presence of other urease producing bacteria in the stomach cannot be denied. Moreover, RUT has been reported with poor sensitivity, especially when

the density of the bacterium is low. Isolation of *H. pylori* is essential to investigate its growth requirements, antibiotic susceptibility testing, studying virulence factor to develop vaccine and many more explorations. It has also got several disadvantages, *i.e*., special conditions for transporting, media, incubation and few days waiting for the colonies to appear, apart from the speed essentially needed to process the specimens. (Patel et al., 2014)

Guidance for H. pylori testing based on clinical features and presentation can be found in various medical society guidelines including but not limited to American College of Gastroenterology, European Society for Paediatric Gastroenterology, Hepatology and Nutrition, North American Society for Pediatric Gastroenterology, Hepatology and Nutrition, and World Gastroenterology Organization.

III. CENTERS FOR MEDICARE & MEDICAID SERVICES (CMS) COVERAGE DETERMINATION

Any applicable federal or state mandates will take precedence over this medical coverage policy.

Medicare: Refer to the CMS Online Manual System (IOMs) and Transmittals. For the most current applicable CMS National Coverage Determination (NCD)/Local Coverage Determination (LCD)/Local Coverage Article (LCA) refer to CMS Medicare Coverage Database.

The information below is current as of the review date for this policy. However, the coverage issues and policies maintained by CMS are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. MAC jurisdiction for purposes of local coverage determinations is governed by the geographic service area where the Medicare Advantage plan is contracted to provide the service. Please refer to the Medicare Coverage Database website for the most current applicable NCD, LCD, LCA, and CMS Online Manual System/Transmittals.

National Coverage Determinations (NCDs)	
National Coverage Determinations (NCDs)	[NCD # and title hyperlink]
Local Coverage Determinations (LCDs)	
MolDX	Prometheus® IBD sgi Diagnostic® Policy - L37299

IV. GUIDELINES/ POSITION STATEMENTS

Medical/Professional Society	Guideline
American College of Gastroenterology	Guidelines Update: Diagnosis and Management of Celiac Disease (2023)
The American College of Gastroenterology	Ulcerative Colitis Practice Guidelines in Adults (2019)
American College of Gastroenterology	Clinical Guideline: Small Intestinal Bacterial Overgrowth (2020)
American Gastroenterological Association	Clinical Guidelines for Therapeutic Drug Monitoring in Inflammatory Bowel Disease (2017)
The American College of Gastroenterology (AGA)	Practice Guidelines for Management of Crohn's disease in adults (2018)
Consensus group on hydrogen and methane-based breath testing	Hydrogen and Methane-Based Breath Testing in Gastrointestinal Disorders: The North American Consensus (2017)
Houston Consensus Conference on Testing for Helicobacter pylori Infection in the United States	Conference on Testing for Helicobacter pylori Infection in the United States (2018)
European Society for Paediatric Gastroenterology, Hepatology and Nutrition, North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN/NASPGHAN)	Guidelines for Management of Helicobacter pylori Infection in Children and Adolescents (2023)
American College of Gastroenterology (ACG)	Treatment of Helicobacter pylori Infection (2024)
World Gastroenterology Organization (WGO)	Helicobacter pylori World Gastroenterology Organization Global Guideline (2023)
The U.S. Preventive Services Task Force (USPSTF)	Celiac Disease: Screening (2017)

V. MEDICAL NECESSITY REVIEW

Prior authorization for certain drug, services, and procedures may or may not be required. In cases where prior authorization is required, providers will submit a request demonstrating that a drug, service, or procedure is medically necessary. For more information, please refer to the Priority Health Provider Manual.

All tests performed at non-participating laboratories will require prior authorization; and as indicated.

VI. APPLICATION TO PRODUCTS

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

- **HMO/EPO:** ***This policy applies to insured HMO/EPO plans.***
- **POS:** ***This policy applies to insured POS plans.***
- **PPO:** ***This policy applies to insured PPO plans. Consult individual plan documents as state mandated benefits may apply. If there is a conflict between this policy and a plan document, the provisions of the plan document will govern.***
- **ASO:** ***For self-funded plans, consult individual plan documents. If there is a conflict between this policy and a self-funded plan document, the provisions of the plan document will govern.***
- **INDIVIDUAL:** ***For individual policies, consult the individual insurance policy. If there is a conflict between this medical policy and the individual insurance policy document, the provisions of the individual insurance policy will govern.***
- **MEDICARE:** ***Coverage is determined by the Centers for Medicare and Medicaid Services (CMS) and/or the Evidence of Coverage (EOC); if a coverage determination has not been adopted by CMS, this policy applies.***
- **MEDICAID/HEALTHY MICHIGAN PLAN:** ***For Medicaid/Healthy Michigan Plan members, this policy will apply. Coverage is based on medical necessity criteria being met and the appropriate code(s) from the coding section of this policy being included on the Michigan Medicaid Fee Schedule located at: http://www.michigan.gov/mdch/0,1607,7-132-2945_42542_42543_42546_42551-159815--,00.html. If there is a discrepancy between this policy and the Michigan Medicaid Provider Manual located at: http://www.michigan.gov/mdch/0,1607,7-132-2945_5100-87572--,00.html, the Michigan Medicaid Provider Manual will govern. For Medical Supplies/DME/Prosthetics and Orthotics, please refer to the Michigan Medicaid Fee Schedule to verify coverage.***

V. CODING INFORMATION

ICD-10 Codes that <u>may</u> apply:

D50.0	Iron deficiency anemia secondary to blood loss (chronic)
D63.8	Anemia in other chronic diseases classified elsewhere
K50.00 – K50.919	Crohn's disease
K51.00 – K51.919	Ulcerative colitis
K52.2X	Allergic and dietetic gastroenteritis and colitis
K52.89	Other specified noninfective gastroenteritis and colitis
K52.9	Noninfective gastroenteritis and colitis, unspecified
K58.0 – K58.9	Irritable bowel syndrome
K59.8X	Other specified functional intestinal disorders
K59.9	Functional intestinal disorder, unspecified
K90.0	Celiac disease
K90.1	Tropical sprue
K90.41	Non-celiac gluten sensitivity

K90.49	Malabsorption due to intolerance, not elsewhere classified
K90.89	Other intestinal malabsorption
K90.9	Intestinal malabsorption, unspecified
K92.1	Melena
K92.2	Gastrointestinal hemorrhage, unspecified
P78.9	Perinatal digestive system disorder, unspecified
R11.0 – R11.2	Nausea and vomiting
R19.4	Change in bowel habit
R19.5	Other fecal abnormalities
R19.7	Diarrhea, unspecified
R19.8	Other specified symptoms and signs involving the digestive system and abdomen
R63.8	Other symptoms and signs concerning food and fluid intake
R93.5	Abnormal findings on diagnostic imaging of other abdominal regions, including retroperitoneum

CPT/HCPCS Codes:

Codes are covered or not covered based on indications in this policy:

81375	HLA Class II typing, low resolution (eg, antigen equivalents); HLA-DRB1/3/4/5 and -DQB1
81382	HLA Class II typing, high resolution (i.e., alleles or allele groups); one locus (eg, HLA-DRB1, -DRB3/4/5, -DQB1, -DQA1, -DPB1, or -DPA1), each
81383	HLA Class II typing, high resolution (ie, alleles or allele groups); 1 allele or allele group (eg, HLA-DQB1*06:02P), each
81335	TPMT (thiopurine S-methyltransferase) (e.g., drug metabolism), gene analysis, common variants (e.g., *2, *3) ***PA through eviCore.*** *Not covered for Medicaid*
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) *(not covered if billed for Crohn's Prognostic)*
81479	Unlisted molecular pathology procedure *(Explanatory note must accompany claim) (not covered if billed for IBD sig Diagnostic)*
81596	Infectious disease, chronic hepatitis C virus (HCV) infection, six biochemical assays (ALT, A2-macroglobulin, apolipoprotein A-1, total bilirubin, GGT, and haptoglobin) utilizing serum, prognostic algorithm reported as scores for fibrosis and necroinflammatory activity in liver
82397	Chemiluminescent assay (*not covered if billed for IBD sig Diagnostic)*
82542	Column chromatography, includes mass spectrometry, if performed (eg, HPLC, LC, LC/MS, LC/MS-MS, GC, GC/MS-MS, GC/MS, HPLC/MS), non-drug analyte(s) not elsewhere specified, qualitative or quantitative, each specimen
82552	Creatine kinase (CK), (CPK); isoenzymes
82657	Enzyme activity in blood cells, cultured cells, or tissue, not elsewhere specified; nonradioactive substrate, each specimen *Not covered for Medicaid*
82784	Gammaglobulin (immunoglobulin); IgA, IgD, IgG, IgM, each
83516	Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; qualitative or semiquantitative, multiple step method
83519	Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; quantitative, by radioimmunoassay (e.g., RIA)

83520	Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; quantitative, not otherwise specified (*not covered if billed for IBD sig Diagnostic and/or Crohn's Prognostic)*
83993	Calprotectin, fecal
84433	Thiopurine S-methyltransferase (TPMT)
84620	Xylose absorption test, blood and/or urine
84999	Unlisted chemistry procedure
81599	Unlisted multianalyte assay with algorithmic analysis (*Explanatory notes must accompany claims billed with unlisted codes.)*
86021	Antibody identification; leukocyte antibodies *(not covered if billed for Crohn's Prognostic)*
86140	C-reactive protein (*not covered if billed for IBD sig Diagnostic)*
86231	Endomysial antibody (EMA), each immunoglobulin (Ig) class86
86255	Fluorescent noninfectious agent antibody; screen, each antibody (*not covered if billed for IBD sig Diagnostic and/or Crohn's Prognostic)*
86256	Fluorescent noninfectious agent antibody; titer, each antibody
86258	Gliadin (deamidated) (DGP) antibody, each immunoglobulin (Ig) class
86364	Tissue transglutaminase, each immunoglobulin (Ig) class
88344	Immunohistochemistry or immunocytochemistry, per specimen; each multiplex antibody stain procedure
88346	Immunofluorescence, per specimen; initial single antibody stain procedure (*not covered if billed for IBD sig Diagnostic)*
88350	Immunofluorescence, per specimen; each additional single antibody stain procedure (List separately in addition to code for primary procedure) (*not covered if billed for IBD sig Diagnostic)*
0034U	TPMT (thiopurine S-methyltransferase), NUDT15 (nudix hydroxylase 15) (e.g., thiopurine metabolism), gene analysis, common variants (i.e., TPMT *2, *3A, *3B, *3C, *4, *5, *6, *8, *12; NUDT15 *3, *4, *5)
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
0286U	CEP72 (centrosomal protein, 72-KDa), NUDT15 (nudix hydrolase 15) and TPMT (thiopurine S-methyltransferase) (eg, drug metabolism) gene analysis, common variants
0430U	Gastroenterology, malabsorption evaluation of alpha-1-antitrypsin, calprotectin, pancreatic elastase and reducing substances, feces, quantitative *(Not Covered)*
0514U	Gastroenterology (irritable bowel disease [IBD]), immunoassay for quantitative determination of adalimumab (ADL) levels in venous serum in patients undergoing adalimumab therapy, results reported as a numerical value as micrograms per milliliter (µg/mL)
0515U	Gastroenterology (irritable bowel disease [IBD]), immunoassay for quantitative determination of infliximab (IFX) levels in venous serum in patients undergoing infliximab therapy, results reported as a numerical value as micrograms per milliliter (µg/mL)

Breath Tests

ICD-10 Codes

Diagnosis codes not covered:

A04.9 - Bacterial intestinal infection, unspecified
K52.9 - Noninfective gastroenteritis and colitis, unspecified
K59.04 - Chronic idiopathic constipation
R63.4 - Abnormal weight loss
K90.9 - Intestinal malabsorption, unspecified
Z00.00 - Encounter for general adult medical examination without abnormal findings

CPT/HCPCS Codes:
91065 Breath hydrogen or methane test (e.g., for detection of lactase deficiency, fructose intolerance, bacterial overgrowth, or oro-cecal gastrointestinal transit)

VI. REFERENCES

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