Additions:
- Pg. 1, Section I, A, 1, criteria updated to reflect vedolizumab (VDZ) and Anser VDZ are a covered benefit.

I. POLICY/Criteria

A. Inflammatory digestive disorders
1. Measurements of serum infliximab (IFX) or adalimumab (ADA) or vedolizumab (VDZ) and antibody to infliximab (ATI) or adalimumab or vedolizumab (e.g. PROMETHEUS® Anser™nIFX / Anser ADA/Anser VDZ) are a covered benefit.
2. 6-thioguanine nucleotide (6-TGN) and 6-methylmercaptopurine nucleotide (6-MMPN) (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.
3. Fecal measurement of calprotectin is a covered benefit for the management of inflammatory bowel diseases (e.g. Crohn's disease, ulcerative colitis). It is not a covered benefit for other indications because its clinical value has not been established.
4. The following tests are experimental and investigational because their clinical value has not been established.
   - Crohn's disease peptide antibody testing
   - ECM1 and Stat-3 testing for ulcerative colitis
   - Measurement of serum mannose-binding lectin
   - Myeloperoxidase antibody testing for inflammatory bowel disease,
   - Proteinase-3 antibody testing,
   - Raman spectroscopy for inflammatory bowel disease.

B. Celiac Disease
1. Serological testing of anti-gliadin antibodies (AGA), anti-reticulin antibodies (ARA), 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 considered to be medically necessary for persons with symptoms suggestive of celiac disease and a serum IgA deficiency.

3. Deamidated gliadin antibodies (DGP) are experimental and investigational as serological markers for celiac disease.

4. Serological tests individually or as part of a panel for celiac disease (IgA-AGA, IgG-AGA, IgA-TTG, and IgA-EMA) are experimental and investigational as an alternative to biopsy for assessing mucosal damage in individuals with celiac disease, and for all other indications (i.e. PROMETHEUS® Celiac PLUS, PROMETHEUS® Celiac Serology).

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 considered to be 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):
   - D-xylose and/or lactulose absorption test
   - Intestinal permeability tests
   - Salivary tests
   - Small-bowel follow-through (barium follow-through examination)
   - Stool studies.

II. MEDICAL NECESSITY REVIEW

☒ All tests performed at non-participating laboratories will require prior authorization.

III. 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.
IV. DESCRIPTION

The American College of Gastroenterology Practice Guidelines for Management of Crohn’s disease in adults (Lichtenstein et al., 2009) state that serological studies evaluating antibodies against Saccharomyces cerevisiae, antineutrophil cytoplasmic antibodies, antibodies directed against CBir1, OmpC 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 a screening tool.

The American College of Gastroenterology Ulcerative Colitis Practice Guidelines in Adults, updated in 2010, states that pANCA have been identified in 60–70% of UC patients but are also found in up to 40% of patients with CD. These pANCA-positive CD patients typically have a clinical phenotype resembling left-sided UC patients, so ANCA detection alone is of little value in distinguishing between UC and CD. The low sensitivity of pANCA for the diagnosis of UC prevents it from serving as a useful diagnostic tool. These assays may be useful, however, in the occasional patient in whom no other clinical or pathologic features allow a diagnostic distinction between UC and Crohn’s colitis.

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.
V. CODING INFORMATION

ICD-10 Codes that may 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
K52.2   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
K59.8   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:

81382   HLA Class II typing, high resolution (ie, alleles or allele groups); one locus (eg, HLA-DRB1, -DRB3/4/5, -DQB1, -DQA1, -DPB1, or -DPA1), each
82397   Chemiluminescent assay
82491   Chromatography, quantitative, column (eg, gas liquid or HPLC); single analyte not elsewhere specified, single stationary and mobile phase
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 (Not Covered for Medicaid)
82657   Enzyme activity in blood cells, cultured cells, or tissue, not elsewhere specified; nonradioactive substrate, each specimen
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 (eg, RIA)
83520 Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; quantitative, not otherwise specified

83993 Calprotectin, fecal
84620 Xylose absorption test, blood and/or urine

84999 Unlisted chemistry procedure (Explanatory notes must accompany claims billed with unlisted codes.) - when billed for Anser® tests

86021 Antibody identification; leukocyte antibodies
86140 C-reactive protein
86255 Fluorescent noninfectious agent antibody; screen, each antibody
86256 Fluorescent noninfectious agent antibody; titer, each antibody

88344 Immunohistochemistry or immunocytochemistry, per specimen; each multiplex antibody stain procedure
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)

VI. REFERENCES

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