

MEDICAL POLICY		Celiac Disease: Serologic Testing	
Effective Date: 07/01/2020  7/1/2020		Section: LAB	Policy No: 404
		Medical Policy Committee Approved Date: 12/17; 12/18; 5/19; 06/2020	
Medical Officer	Date		

See Policy CPT CODE section below for any prior authorization requirements

SCOPE:

Providence Health Plan, Providence Health Assurance, Providence Plan Partners, and Ayin Health Solutions as applicable (referred to individually as “Company” and collectively as “Companies”).

APPLIES TO:

All lines of business

BENEFIT APPLICATION

Medicaid Members

Oregon: Services requested for Oregon Health Plan (OHP) members follow the OHP Prioritized List and Oregon Administrative Rules (OARs) as the primary resource for coverage determinations. Medical policy criteria below may be applied when there are no criteria available in the OARs and the OHP Prioritized List.

POLICY CRITERIA

- I. HLA-DQ2/DQ8 genotype testing (i.e., Prometheus Celiac Genetics) may be considered **medically necessary and covered** when **both** of the following criteria (A. and B.) are met:
 - A. The genotyping is used to effectively rule out celiac disease; **and**
 - B. The patient meets **at least one** of the following (1.-5.) clinical situations:
 1. Equivocal small-bowel histological findings (Marsh I-II) in seronegative patients; **or**
 2. Evaluation of patients on a gluten-free diet (GFD) in whom no testing for CD was done before GFD; **or**
 3. Patients with discrepant celiac-specific serology and histology; **or**
 4. Patients with suspicion of refractory CD where the original diagnosis of celiac disease remains in question; **or**
 5. Patient with Down’s syndrome.
- II. HLA-DQ2/DQ8 genotype testing (i.e., Prometheus Celiac Genetics) is considered **not medically necessary and is not covered** when criterion I. above is not met.

- III. The use of a comprehensive multi-marker panel serum antibody profile test (i.e., Prometheus Celiac Serology) is considered **not medically necessary and is not covered** for the screening or diagnosis of celiac disease.
- IV. The use of a combination panel, including antibody and genetic markers (i.e., Prometheus Celiac Plus) is considered **not medically necessary and is not covered** for the screening or diagnosis of celiac disease.

Link to [Policy Summary](#)

BILLING GUIDELINES

If CPT codes 82784, 83520, and 88346 are billed in conjunction with 81382 (i.e., Prometheus Celiac Plus) this will deny as not medically necessary and not covered (see criterion IV. above).

If CPT codes 82784, 83520, and 88346 are billed together (i.e., Prometheus Celiac Serology) these will deny as not medically necessary and not covered (see criterion III. above).

CPT CODES

All Lines of Business

Prior Authorization Required

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
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DESCRIPTION

Celiac Disease

Celiac disease is an autoimmune disorder in which the ingestion of gluten, found in wheat-, rye-, and barley-containing products, leads to progressive damage of the mucosal lining of the small intestine. The common symptoms associated with celiac disease include malabsorption, chronic diarrhea, and failure to thrive; however, the clinical manifestations can be extremely variable and many individuals present with symptoms unrelated to the digestive system. Typically, the presence of specific antibodies (antigliadin, antiendomysial, and antitissue transglutaminase), histological findings on small bowel biopsy, and a positive response to a gluten-free diet are used to diagnose celiac disease.

HLA-DQ Genotyping

Celiac disease results from the interactions of 2 human leukocyte antigen (HLA) genes with non-HLA genes. Approximately 90% to 95% of individuals with celiac disease carry the DQA or DQB allele, and express the DQ2 HLA molecule. The remaining 5% to 10% of individuals with celiac disease express the DQ8 HLA molecule. HLA-DQ genotyping is typically performed using polymerase chain reaction (PCR) amplification with sequence-specific primers (PCR-SSP) or PCR with hybridization of sequence-specific

probes to detect the HLA-DQA1 and HLA-DQB1 gene variants known to be associated with celiac disease: DQA1*0501, DQA*0505, DQB1*0201, DQB1*0202, DQA1*0301, and DQB1*0302.

REVIEW OF EVIDENCE

A review of the ECRI, Hayes, Cochrane, and PubMed databases was conducted regarding the use of serologic testing to diagnose celiac disease. Below is a summary of the available evidence identified through May 2020.

Due to a large and extensive body of literature, the evidence supporting the medical necessity of serologic testing for celiac disease is based on the American College of Gastroenterology evidence-based clinical practice guidelines.

CLINICAL PRACTICE GUIDELINES

American College of Gastroenterology (ACG)

The 2013 evidence-based ACG guidelines for the diagnosis and management of celiac disease (CD) gave the following recommendations for the diagnosis of CD: ¹

1. Immunoglobulin A (IgA) anti-tissue transglutaminase (TTG) antibody is the preferred single test for detection of CD in individuals over the age of 2 years (strong recommendation, high level of evidence).
2. When there exists a high probability of CD wherein the possibility of IgA deficiency is considered, total IgA should be measured. An alternative approach is to include both IgA and immunoglobulin G (IgG) based testing, such as IgG-deamidated gliadin peptides (DGPs), in these high-probability patients (strong recommendation, moderate level of evidence).
3. In patients in whom low IgA or selective IgA deficiency is identified, IgG-based testing (IgG DGPs and IgG TTG) should be performed (strong recommendation, moderate level of evidence).
4. If the suspicion of CD is high, intestinal biopsy should be pursued even if serologies are negative (strong recommendation, moderate level of evidence).
5. All diagnostic serologic testing should be done with patients on a gluten-containing diet (strong recommendation, high level of evidence).
6. Antibodies directed against native gliadin are not recommended for the primary detection of CD. (strong recommendation, high level of evidence).
7. Combining several tests for CD in lieu of TTG IgA alone may marginally increase the sensitivity for CD but reduces specificity and therefore are not recommended in low-risk populations (conditional recommendation, moderate level of evidence).
8. When screening children younger than 2 years of age for CD, the IgA TTG test should be combined with DGP (IgA and IgG) (strong recommendation, moderate level of evidence).

The guideline gave the following recommendations regarding the diagnosis of celiac disease (CD) in patients on a gluten-free diet (GFD):

1. While standard diagnostic tests (specific serology and intestinal biopsy) have a high positive predictive value (PPV) for CD, they should not be relied upon to exclude CD in patients already adhering to a GFD (strong recommendation, high level of evidence).
2. HLA-DQ2/DQ8 genotyping should be used to try to exclude CD prior to embarking on a formal gluten challenge (strong recommendation, high level of evidence).
3. Formal gluten challenge should be considered, where necessary, to diagnose or exclude CD in patients already adhering to a GFD (strong recommendation, high level of evidence).

The ACG guideline also gave the following recommendations regarding HLA-DQ2/DQ8 testing:

1. HLA-DQ2/DQ8 testing should not be used routinely in the initial diagnosis of CD (Strong recommendation, moderate level of evidence).
2. HLA-DQ2/DQ8 genotyping testing should be used to effectively rule out the disease in selected clinical situations (Strong recommendation, moderate level of evidence).
3. Examples of such clinical situations include but are not limited to:
 - a. Equivocal small-bowel histological finding (Marsh I-II) in seronegative patients
 - b. Evaluation of patients on a gluten-free diet (GFD) in whom no testing for CD was done before GFD
 - c. Patients with discrepant celiac-specific serology and histology
 - d. Patients with suspicion of refractory CD where the original diagnosis of celiac remains in question
 - e. Patients with Down's syndrome

U.S. Preventive Services Task Force (USPSTF)

The 2017 evidence-based USPSTF recommendation regarding screening asymptomatic adults, adolescents, and children for celiac disease stated, “the current evidence is insufficient to assess the balance of benefits and harms of screening for celiac disease in asymptomatic persons.”²

CENTERS FOR MEDICARE & MEDICAID

As of May 2020, no Centers for Medicare & Medicaid (CMS) coverage guidance was identified which addresses serologic testing for celiac disease.

POLICY SUMMARY

The American College of Gastroenterology (ACG) recommends the use of HLA-DQ2/DQ8 testing when selected clinical situations are met. The ACG also states that Immunoglobulin A (IgA) anti-tissue transglutaminase (TTG) antibody is the preferred single test for detection of celiac disease, and that the combination of several tests may marginally increase the sensitivity but reduces the specificity; therefore, combination testing is considered not medically necessary.

INSTRUCTIONS FOR USE

Company Medical Policies serve as guidance for the administration of plan benefits. Medical policies do not constitute medical advice nor a guarantee of coverage. Company Medical Policies are reviewed

annually and are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. The Companies reserve the right to determine the application of Medical Policies and make revisions to Medical Policies at any time. Providers will be given at least 60-days notice of policy changes that are restrictive in nature.

The scope and availability of all plan benefits are determined in accordance with the applicable coverage agreement. Any conflict or variance between the terms of the coverage agreement and Company Medical Policy will be resolved in favor of the coverage agreement.

REGULATORY STATUS

Mental Health Parity Statement

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.

MEDICAL POLICY CROSS REFERENCES

- Inflammatory Bowel Disease: Serologic Testing and Therapeutic Monitoring
- Inflammatory Bowel Disease: Measurement of Antibodies to Immunosuppressive Therapies

REFERENCES

1. Rubio-Tapia A, Hill ID, Kelly CP, Calderwood AH, Murray JA. ACG clinical guidelines: diagnosis and management of celiac disease. *The American journal of gastroenterology*. 2013;108(5):656. http://gi.org/wp-content/uploads/2013/05/ACG_Guideline_CeliacDisease_May_2013.pdf
2. U.S. Food and Drug Administration Summary of Safety and Effectiveness Data: Hyalgan. https://www.accessdata.fda.gov/cdrh_docs/pdf/P950027A.pdf. Published 1997. Accessed 8/9/2017.