of Tennessee

Policy

Reimbursement Policy

Celiac Disease Testing

I. Policy Description

Celiac disease is a hereditary, chronic autoimmune disorder triggered by the ingestion of gluten, a protein found in wheat, rye, and barley. When an individual with celiac disease ingests gluten, the body mounts an immune response that attacks the small intestine. These attacks lead to damage on the villi within the small intestine, inhibiting nutrient absorption (CDF, 2024).

II. Indications and/or Limitations of Coverage

Application of coverage criteria is dependent upon an individual's benefit coverage at the time of the request. Specifications pertaining to Medicare and Medicaid can be found in in the "Applicable State and Federal Regulations" section of this policy document.

1) For individuals who have been diagnosed with celiac disease and who are IgA sufficient, serologic testing with IgA anti-tissue transglutaminase (TTG) **MEETS COVERAGE CRITERIA** at the following intervals:
   a) At the first follow-up visit 3-6 months after diagnosis.
   b) Every 6 months until normalization of anti-TTG levels has occurred.
   c) Every 12-24 months thereafter.

2) For individuals who have been diagnosed with celiac disease and who are IgA deficient, testing for IgG endomysial antibodies, IgG deamidated gliadin peptide, or IgG TTG **MEETS COVERAGE CRITERIA** at the following intervals:
   a) At the first follow-up visit 3-6 months after diagnosis.
   b) Every 6 months until normalization of IgG levels has occurred.
   c) Every 12-24 months thereafter.

3) For individuals with signs and symptoms of celiac disease (see Note 1), serologic testing with the IgA anti-TTG **and** the total IgA test for the diagnosis of celiac disease **MEETS COVERAGE CRITERIA**.

4) For individuals at risk for celiac disease (see Note 1), when IgA anti-TTG is negative or weakly positive, testing for IgA endomysial antibodies **MEETS COVERAGE CRITERIA**.

Reimbursement Policy

5) For individuals with clinical suspicion of celiac disease (see Note 1) with an IgA deficiency, testing for IgG endomysial antibodies, IgG deamidated gliadin peptide, **or** IgG TTG **MEETS COVERAGE CRITERIA**.

6) Testing for IgA and IgG antibodies to deamidated gliadin peptides **MEETS COVERAGE CRITERIA** in **any** of the following situations**:**

   a) For individuals under 2 years of age with a clinical suspicion of celiac disease (see Note 1).

   b) For individuals over 2 years of age as a substitute for anti-TTG testing.

7) Genetic testing for HLA DQ2 and DQ8 **MEETS COVERAGE CRITERIA** in **any** of the following situations:

   a) For symptomatic individuals for whom other testing is undiagnostic.

   b) For symptomatic individuals with positive serology tests who are unable to undergo a biopsy evaluation.

8) For confirmation of celiac disease in individuals at high risk for celiac disease, regardless of the result of celiac disease serology testing, pathological examination of tissue obtained from a biopsy of the small intestine **MEETS COVERAGE CRITERIA**.

9) Rapid antigen point-of-care testing for anti-TTG **DOES NOT MEET COVERAGE CRITERIA**.

10) Panel testing, multiplex testing, or multi-analyte testing (for more than two analytes) for the diagnosis or evaluation of celiac disease **DOES NOT MEET COVERAGE CRITERIA**.

11) For asymptomatic individuals not at an increased risk for developing celiac disease (see Note 1), testing for celiac disease **DOES NOT MEET COVERAGE CRITERIA.**

The following does not meet coverage criteria due to a lack of available published scientific literature confirming that the test(s) is/are required and beneficial for the diagnosis and treatment of an individual's illness.

12) For the diagnosis of celiac disease, testing for anti-reticulin antibodies **DOES NOT MEET COVERAGE CRITERIA**.

13) For the evaluation of celiac disease, testing of stool or saliva samples **DOES NOT MEET COVERAGE CRITERIA**.

14) Serologic testing using an HLA-DQ-gluten tetramer-based assay, including flow cytometry-based HLA-DQ-gluten tetramer assays, **DOES NOT MEET COVERAGE CRITERIA**.

NOTES:

Note 1: Signs and symptoms of celiac disease may include, but are not limited to, the following: unexplained chronic or intermittent diarrhea; unexplained weight loss; unexplained chronic or intermittent abdominal pain or bloating; recurrent nausea or vomiting; unexplained iron deficiency anemia; unexplained vitamin B12 or folate deficiency; unexplained liver transaminase elevations; autoimmune hepatitis; dermatitis herpetiformis; type 1 diabetes; intestinal blockages; unexplained subfertility or miscarriage; unexplained osteoporosis, osteomalacia, or low bone density; and/or primary biliary cirrhosis. Individuals with Down syndrome, Turner syndrome, or Williams-Beuren syndrome are also at high risk for celiac disease. Additionally, in pediatric patients, fatty stools, delayed puberty, amenorrhea, failure to thrive, stunted growth, and/or short stature may also be associated with celiac disease (Husby et al., 2020; NICE, 2022; NIDDK, 2016).

III. Applicable State and Federal Regulations

DISCLAIMER: If there is a conflict between this Policy and any relevant, applicable government policy for a particular member [e.g., Local Coverage Determinations (LCDs) or National Coverage Determinations (NCDs) for Medicare and/or state coverage for Medicaid], then the government policy will be used to make the determination. For the most up-to-date Medicare policies and coverage, please visit the Medicare search website: https://www.cms.gov/medicare-coverage-database/search.aspx. For the most up-to-date Medicaid policies and coverage, visit the applicable state Medicaid website.

Food and Drug Administration (FDA)

The Quanta Lite Celiac Screen ELISA test for tissue transglutaminase/gliadin and the Quanta Lite Celiac DGP Screen by Inova Diagnostics, Inc. were approved by the FDA on 01/28/1999 and 12/13/2006, respectively. Quanta Plex Celiac IgA and IgG profiles by Inova Diagnostics, Inc. were approved on 03/14/2007 and 06/20/2007.

EliA Celikey IgG for use with the EliA Celikey IgG Immunoassay by Phadia US, Inc. was approved by the FDA on 12/26/2006.

The FIDIS Celiac on the FIDS Analyser and FIDIS CELIAC kit by Biomedical Diagnostics S.A. were approved by the FDA on 09/24/2004 and 03/29/2006, respectively.

The IMMULISA CELIAC ELISA testing systems for gliadin IgA/IgG and TTG IgA/IgG by IMMCO Diagnostics, Inc. were approved on 02/04/2010 and 03/10/2010. IMMCO's IMMULISA enhanced celiac fusion (TTG/DGP) IgA/IgG antibody ELISA system was approved on 10/25/2013.

Reimbursement Policy

Bio-Rad Laboratories' Bioplex 2200 Celiac IgA IgG kits were approved on 09/19/2013. The IgX Plex Celiac qualitative assay and Ig Plex Celiac DG panel by SQI diagnostics systems, Inc. were approved by the FDA on 06/02/2011 and 11/06/2014, respectively.

SQI Diagnostics received FDA clearance for the Ig plex Celiac DGP which detects IgA and IgG antibodies to deamidated gliadin peptide (DGP) and tissue transglutaminase (tTG) in human serum. This was approved by the FDA on Nov 06, 2014 (FDA, 2014).

Inova Diagnostics received FDA clearance on June 16, 2021, for the Aptiva Celiac Disease IgA Reagent, which is an "immunoassay utilizing particle-based multi-analyte technology for the semi-quantitative determination of anti-tissue transglutaminase IgA autoantibodies and anti-deamidated gliadin peptide IgA antibodies in human serum." They also received approval for an IgG Reagent in 2021. It can be used to diagnose celiac disease and dermatitis herpetiformis (FDA, 2021).

No nucleic acid-based test solely for celiac disease has been approved by the FDA as of July 2019. The FDA has approved the direct-to-consumer panel test by 23andme that includes a single nucleotide polymorphism in HLA-DQA1 (FDA, 2017).

Many labs have developed specific tests that they must validate and perform in house. These laboratory-developed tests (LDTs) are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88). LDTs are not approved or cleared by the U. S. Food and Drug Administration; however, FDA clearance or approval is not currently required for clinical use.

IV. Applicable CPT/HCPCS Procedure Codes

CPT	Code Description
81376	HLA Class II typing, low resolution (eg, antigen equivalents); one locus (eg, HLA-DRB1, -DRB3/4/5, -DQB1, -DQA1, -DPB1, or -DPA1), each
81377	HLA Class II typing, low resolution (eg, antigen equivalents); one antigen equivalent, each
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
81383	HLA Class II typing, high resolution (ie, alleles or allele groups); one allele or allele group (eg, HLA-DQB1*06:02P), each
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
86231	Endomysial antibody (EMA), each immunoglobulin (Ig) class
86255	Fluorescent noninfectious agent antibody; screen, each antibody

86256	Fluorescent noninfectious agent antibody; titer, each antibody
86258	Gliadin (deamidated) (DGP) antibody, each immunoglobulin (Ig) class
86364	Tissue transglutaminase, each immunoglobulin (Ig) class
88305	Level IV - Surgical pathology, gross and microscopic examination, colon biopsy

Procedure codes appearing in Medical Policy documents are included only as a general reference tool for each policy. They may not be all-inclusive.

V. Evidence-based Scientific References

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Reimbursement Policy

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