

WellCare Health Plans, Inc.
The WellCare Group of Companies

Clinical Coverage Guideline



WellCare Prescription Insurance, Inc.

*'Ohana Health Plan, a plan offered by
WellCare Health Insurance of Arizona, Inc.*



WellCare Health Insurance of Illinois, Inc.

WellCare Health Insurance of New York, Inc.

Harmony Behavioral Health, Inc.

Harmony Behavioral Health of Florida, Inc.

WellCare of Texas, Inc.

WellCare Health Plans of New Jersey, Inc.

WellCare of Florida, Inc.

HealthEase of Florida, Inc.

WellCare of Louisiana, Inc.

WellCare of New York, Inc.

WellCare of Connecticut, Inc.

WellCare of Georgia, Inc.

Harmony Health Plan of Illinois, Inc.

WellCare of Ohio, Inc.

Celiac Disease DNA Testing

Guideline Number: HS-163

Original Effective Date: 4/1/2010

Revision Date: n/a

The Clinical Coverage Guideline is intended to supplement certain standard WellCare benefit plans. The terms of a member's particular Benefit Plan, Evidence of Coverage, Certificate of Coverage, etc., may differ significantly from this Coverage Position. For example, a member's benefit plan may contain specific exclusions related to the topic addressed in this Clinical Coverage Guideline. When a conflict exists between the two documents, the Member's Benefit Plan always supersedes the information contained in the Clinical Coverage Guideline. Additionally, Clinical Coverage Guidelines relate exclusively to the administration of health benefit plans and are NOT recommendations for treatment, nor should they be used as treatment guidelines. The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any.

Clinical Coverage Guideline HS-163

Celiac Disease DNA Testing

Original Effective Date: 4/1/2010

Revised Date(s): n/a

DISCLAIMER

The Clinical Coverage Guideline is intended to supplement certain standard WellCare benefit plans. The terms of a member's particular Benefit Plan, Evidence of Coverage, Certificate of Coverage, etc., may differ significantly from this Coverage Position. For example, a member's benefit plan may contain specific exclusions related to the topic addressed in this Clinical Coverage Guideline. When a conflict exists between the two documents, the Member's Benefit Plan always supersedes the information contained in the Clinical Coverage Guideline. Additionally, Clinical Coverage Guidelines relate exclusively to the administration of health benefit plans and are NOT recommendations for treatment, nor should they be used as treatment guidelines.

APPLICATION STATEMENT

The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any.

CLINICAL COVERAGE GUIDELINE

Celiac disease DNA testing of the HLA-DQA1 and HLA-DQB1 genes is considered medically necessary in the following circumstances:

- For symptomatic members who have not responded to a gluten-free diet; **AND**,
- For symptomatic members with borderline or ambiguous celiac-associated antibody results or small-bowel biopsy results

Celiac disease DNA testing of the HLA-DQA1 and HLA-DQB1 genes is considered NOT medically necessary in the following circumstances:

- For the evaluation or diagnosis confirmation of celiac disease in symptomatic members with an unequivocal diagnosis by small bowel biopsy and serology; **OR**,
- For the pre-symptomatic evaluation of family members of members with confirmed celiac disease; **OR**,
- For the screening of healthy individuals with no family history of celiac disease (i.e., population screening); **OR**,
- Any circumstance not listed in the medically necessary list above.

BACKGROUND

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. It is typically diagnosed based on the presence of specific antibodies (antigliadin, antiendomysial, and antitissue transglutaminase) in the blood of affected individuals, characteristic histological findings on small bowel biopsy, and a positive response to a glutenfree diet. The clinical manifestations associated with celiac disease are extremely variable. While the classic triad of features (malabsorption, chronic diarrhea, and failure to thrive) is common, many individuals with celiac disease present with more atypical symptoms, many of which are unrelated to the digestive system. Gastrointestinal symptoms may include abdominal pain, constipation, weight loss, lactose intolerance, irritable bowel syndrome, and abdominal distention. Nongastrointestinal symptoms may include iron-deficient anemia, dermatitis herpetiformis (a blistering skin rash), chronic

fatigue, joint pain, migraines, infertility, short stature, delayed puberty, psychiatric disorders, and defects of the dental enamel. In addition, patients with celiac disease are at an increased risk for other autoimmune disorders, such as type 1 diabetes mellitus or thyroiditis, and may have an increased risk for certain malignancies, if untreated. Treatment of celiac disease with a gluten-free diet can eliminate the symptoms of the disease and may result in a normalization of small bowel histology.

The prevalence of celiac disease varies by population background, but it is estimated that approximately 1 in 100 Americans has the disease, many of whom remain undiagnosed. Celiac disease is a multifactorial disorder that results from the interactions of 2 human leukocyte antigen (HLA) genes with non-HLA genes and various environmental factors (including gluten exposure). The *HLA-DQA1* and *HLA-DQB1* genes, both of which are located on chromosome 6 at band p21.3, encode the alpha and beta chains of HLA heterodimers. Approximately 90% to 95% of individuals with celiac disease carry either the *DQA1*0501* allele or the *DQA*0505* allele, along with either the *DQB1*0201* allele or the *DQB1*0202* allele, and express the DQ2 HLA molecule. Most of the remaining 5% to 10% of patients carry *DQA1*03* and *DQB1*0302* alleles and express the DQ8 HLA molecule. In individuals with celiac disease, the DQ2 and DQ8 heterodimers bind gluten peptides and present them to T cells, triggering an immune response and subsequent tissue damage in the small intestine. However, DQ2 and DQ8 heterodimers are also found in approximately 25% to 40% of healthy individuals, suggesting that specific HLA genotypes are necessary, but not sufficient, for the development of celiac disease.

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*. Celiac disease gene testing may be considered in children and adults who are exhibiting symptoms of celiac disease but have borderline or ambiguous results from antibody testing and small bowel biopsy. This may include previously symptomatic individuals who are no longer exhibiting symptoms on a gluten-free diet. In addition, testing may be considered in the family members of celiac disease patients. It has also been proposed that *HLA-DQ* genotyping may be used to screen individuals in the general population in order to identify those with undiagnosed celiac disease (Hayes, 2010).

Cost Analysis

Cost for the test ranges from \$395 (Kimball Genetics, Inc.) to \$509 (Prometheus Laboratories).

CODING

Covered CPT® Codes

- 82784** Total Serum IgA, by Nephelometry
- 83520** ASCA (Anti-Saccharomyces cerevisiae) ELISA, **IgA** specific
- 83520** Anti-Gliadin ELISA, **IgG** specific
- 83520** Anti-Human Tissue Transglutaminase (hu-tTG) ELISA, IgA Recombinant antigen
- 83891** Molecular diagnostics; isolation or extraction of highly purified nucleic acid, each nucleic acid type
- 83896** Molecular diagnostics; nucleic acid probe, each; DQA1 and DQB1 (x72)
- 83898** Molecular diagnostics; amplification, target, each nucleic acid sequence
- 83900** Molecular diagnostics; Amplification of patient nucleic acid, multiplex, first two nucleic acid sequences for DQA1
- 83900** Molecular diagnostics; Amplification of patient nucleic acid, multiplex, first two nucleic acid sequences for DQB1
- 83901+** Molecular diagnostics; amplification, target, multiplex, each additional nucleic acid sequence beyond 2
+List separately in addition to code for primary procedure
- 83912** Molecular diagnostics; interpretation and report
- 88347** Anti-Endomysial (EMA) IgA antibody by IFA

ICD-9-CM Procedure Codes

No applicable codes

HCPCS Level II ® Codes

No applicable codes

Covered ICD-9-CM Diagnosis Codes when the above criteria has been met.

579.0 Celiac disease

V18.5 Family history of digestive disorders

V77.99 Special screening for other and unspecified endocrine, nutritional, metabolic, and immunity disorders

*Current Procedural Terminology (CPT®) ©2010 American Medical Association: Chicago, IL.

REFERENCES

1. Hayes GTE Report. Celiac Disease. January 4, 2010.
2. Rostom A, Murray JA, Kagnoff MF. American Gastroenterological Association (AGA) Institute technical review on the diagnosis and management of celiac disease. *Gastroenterology*. 2006;131(6):1981-2002.
3. Megiorni F, Mora B, Bonamico M, et al. HLA-DQ and risk gradient for celiac disease. *Hum Immunol*. 2009;70(1):55-59.
4. Ollikka P, Raussi HM, Laitala V, et al. Genotyping of celiac disease-related-risk haplotypes using a closed-tube polymerase chain reaction analysis of dried blood and saliva disk samples. *Anal Biochem*. 2009;386(1):20-29.
5. Hadithi M, von Blomberg BM, Crusius JB, et al. Accuracy of serologic tests and HLA-DQ typing for diagnosing celiac disease. *Ann Intern Med*. 2007;147(5):294-302.
6. Murray JA, Moore SB, Van Dyke CT, et al. HLA DQ gene dosage and risk and severity of celiac disease. *Clin Gastroenterol Hepatol*. 2007;5(12):1406-1412.