Medical Policy

Human Leukocyte Antigen (HLA) Testing for Celiac Disease

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Policy Number: 567
BCBSA Reference Number: 2.04.95

Related Policies
- Wireless Capsule Endoscopy as a Diagnostic Technique in Disorders of the Small Bowel, Esophagus, and Colon, #185

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO BlueSM and Medicare PPO BlueSM Members

HLA-DQ2 and HLA-DQ8 testing may be considered MEDICALLY NECESSARY to rule out celiac disease in:
- Patients with discordant serologic and histologic (biopsy) findings; or
- Patients with persistent symptoms despite negative serology and histology.

HLA-DQ2 and HLA-DQ8 testing for celiac disease is INVESTIGATIONAL in all other situations.

Prior Authorization Information

Pre-service approval is required for all inpatient services for all products. See below for situations where prior authorization may be required or may not be required for outpatient services.

Yes indicates that prior authorization is required.
No indicates that prior authorization is not required.
N/A indicates that this service is primarily performed in an inpatient setting.

<table>
<thead>
<tr>
<th>Outpatient</th>
<th>Commercial Managed Care (HMO and POS)</th>
<th>No</th>
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<tbody>
<tr>
<td></td>
<td>Commercial PPO and Indemnity</td>
<td>No</td>
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<td>Medicare HMO BlueSM</td>
<td>No</td>
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</table>
CPT Codes / HCPCS Codes / ICD-9 Codes

The following codes are included below for informational purposes. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

<table>
<thead>
<tr>
<th>CPT codes</th>
<th>Code Description</th>
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<tbody>
<tr>
<td>81377</td>
<td>HLA Class II typing, low resolution (eg, antigen equivalents); 1 antigen equivalent, each</td>
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<tr>
<td>81383</td>
<td>HLA Class II typing, high resolution (ie, alleles or allele groups); 1 allele or allele group (eg, HLA-DQB1*06:02P), each</td>
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Description
Celiac disease is currently diagnosed by serologic results in patients and a consistent history with confirmation by small intestinal biopsy. Human leukocyte antigen (HLA) testing may be useful for ruling out disease in symptomatic patients when findings of other tests are inconclusive.

Background
Celiac disease, which is also referred to as celiac sprue or gluten-sensitive enteropathy, is a relatively common disorder that has variable clinical expression. Population-based screening surveys suggest a prevalence of 1 in 250–500 in most countries, including the U.S. However, this prevalence may vary widely depending on how the disease is defined, i.e., whether only clinically apparent cases are considered, as opposed to including all individuals with any serologic or histologic evidence of disease.

Celiac disease is characterized by inflammation of the small intestine resulting from an immunologic intolerance to gluten, i.e., the proteins derived from wheat, barley, and rye. The symptoms of the disease are markedly variable and can be broadly subdivided into intestinal and extraintestinal manifestations; the latter is thought to be related to nutrient malabsorption. For example, osteopenia and osteoporosis, which are commonly seen in adults with untreated celiac disease, are related to the impaired absorption of vitamin D and binding of intraluminal calcium and magnesium to unabsorbed dietary fatty acids, forming insoluble soaps. The only treatment for celiac disease is lifelong adherence to a gluten-free diet.

Many of the symptoms of celiac disease, e.g., diarrhea, abdominal pain and weight loss are nonspecific and are often overlooked. In addition, the disease may develop at any time in life, from infancy to very old age. In children, the disease typically presents following weaning between 6 and 24 months, and is characterized by abnormal stools, poor appetite, and irritability. In adults, diarrhea is the main presenting symptom, but presenting symptoms may be entirely nonspecific, such as anemia or infertility. Typical or classical celiac disease refers to the presence of malabsorption, while atypical celiac disease consists primarily of extraintestinal manifestations.

Celiac disease is a human leukocyte antigen (HLA) -associated disease. Approximately 90% to 95% of patients with celiac disease carry the HLA-DQ2 allele and the remaining 5% to 10% carry the HLA-DQ8 allele. However, not all people with one of these 2 alleles will develop celiac disease. It is believed that approximately 25% to 40% of the general population of the U.S. carries either the HLA-DQ2 or HLA-DQ8 allele but only about 3% of individuals carrying the DQ2/DQ8 alleles will develop gluten intolerance. (1, 2)
Given the nonspecific nature of the symptoms, definitive diagnosis has been based on the results of small intestinal biopsies showing a flattened intestinal mucosa in association with an inflammatory infiltrate. Diagnostic criteria were first established in 1969 by the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHN) and consisted of a series of 3 intestinal biopsies: one at diagnosis, one after institution of a gluten-free diet, and the third after a repeat gluten challenge. This cumbersome method of diagnosis was revised in 1990 by simplifying the diagnostic criteria to a positive biopsy at presentation in conjunction with consistent history and serologic results, followed by a clinical response to a gluten-free diet. (3)

While a positive biopsy result is considered the gold standard for diagnosis, serologic evaluation of patients with possible celiac disease, together with a consistent clinical history and a positive response to a gluten-free diet, can sometimes be adequate for diagnosis. Serologic studies are also useful in triaging the large numbers of patients with nonspecific symptoms for biopsy. In approximately 10% of cases in which clinical suspicion suggests celiac disease, serologic testing and intestinal biopsy are non-diagnostic, either because the results of serology and biopsy are discordant, or because both tests are negative despite persistent symptoms suggestive of celiac disease. In these cases, HLA testing may be useful for ruling out a diagnosis of celiac disease.

Summary
Several studies have reported that the sensitivity and negative predictive value of HLA testing for celiac disease is 100%, meaning that this test is highly accurate for ruling out celiac disease. In contrast, a substantial number of patients who do not have celiac disease carry the HLA-DQ2 and/or HLA-DQ8 alleles, resulting in suboptimal specificity, meaning that this test is less accurate for confirming the diagnosis. National recommendations and study data support the conclusion that HLA typing is useful for ruling out celiac disease when patients have discordant serologic and histologic (biopsy) findings or when patients have persistent symptoms despite negative serology and histology. Thus, HLA typing may be considered medically necessary in these situations and is otherwise considered investigational.

Policy History

<table>
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<tr>
<th>Date</th>
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<tr>
<td>7/2015</td>
<td>New references added from BCBSA National medical policy.</td>
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Information Pertaining to All Blue Cross Blue Shield Medical Policies
Click on any of the following terms to access the relevant information:
- Medical Policy Terms of Use
- Managed Care Guidelines
- Indemnity/PPO Guidelines
- Clinical Exception Process
- Medical Technology Assessment Guidelines

References