Clinical Policy Title: Celiac disease — diagnostic testing

Clinical Policy Number: CCP.1049

Effective Date: December 1, 2013
Initial Review Date: August 21, 2013
Most Recent Review Date: August 7, 2018
Next Review Date: August 2019

Related policies:

CCP.1055 Capsule endoscopy

ABOUT THIS POLICY: Prestige Health Choice has developed clinical policies to assist with making coverage determinations. Prestige Health Choice’s clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by Prestige Health Choice when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Prestige Health Choice’s clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Prestige Health Choice’s clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Prestige Health Choice will update its clinical policies as necessary. Prestige Health Choice’s clinical policies are not guarantees of payment.

Coverage policy

Prestige Health Choice considers serologic testing of immunoglobulin A or G antibodies against endomysial, tissue transglutaminase, and deamidated gliadin peptides to be clinically proven and, therefore, medically necessary for the following indications (Hill, 2016; National Institute for Health and Care Excellence, 2015; Rubio-Tapia, 2013):

- To screen members with signs or symptoms suggestive of celiac disease while on a gluten-containing diet.
- To screen pediatric members for celiac disease who are at increased risk for celiac disease (e.g., first-degree relatives of an index case or people with trisomy 21, Turner syndrome, Williams syndrome, immunoglobulin A deficiency, or other autoimmune conditions) with no, very minor, or less typical symptoms.
- To monitor response to a gluten-free diet in members with celiac disease.
- For annual monitoring once serology has normalized and symptoms have resolved.
Prestige Health Choice considers testing of total serum immunoglobulin A to be clinically proven and, therefore, medically necessary for members with symptoms suggestive of celiac disease and either (Hill, 2016; Rubio-Tapia, 2013):

- Indeterminate screening serology results.
- Suspected immunoglobulin A deficiency.

Prestige Health Choice considers human leukocyte antigen-DQ2 and -DQ8 genetic testing to be clinically proven and, therefore, medically necessary to rule out celiac disease if either (Hill, 2016; National Institute for Health and Care Excellence, 2015; Rubio-Tapia, 2013):

- The member has discordant serologic and histologic biopsy findings.
- The member has persistent symptoms that warrant testing despite negative serology and histology.

Limitations:

Coverage determinations are subject to benefit limitations and exclusions as delineated by the state Medicaid authority. The Florida Medicaid website may be accessed at http://ahca.myflorida.com/Medicaid/.

Serologic tests of anti-reticulin antibodies or anti-gliadin antibodies lack optimal sensitivity and specificity for routine diagnostic use and are not medically necessary.

Frequency of serologic testing for monitoring response to a gluten-free diet is limited to every three to six months, until serology has normalized and symptoms have resolved, after which annual testing is medically necessary (Hill, 2016; Rubio-Tapia, 2013).

All other uses of diagnostic testing for celiac disease are not medically necessary, including (Bibbins-Domingo, 2017; Chou, 2017; Hill, 2016; National Institute for Health and Care Excellence, 2015; Rubio-Tapia, 2013):

- Screening individuals for asymptomatic celiac disease using serologic testing.
- Screening individuals for asymptomatic celiac disease using self-tests and/or point-of-care tests as a substitute for serologic testing.
- Using serologic testing as an alternative to biopsy.
- Using sequential measurement of endomysial antibodies.
- Using human leukocyte antigen-DQ2/DQ8 testing in the initial diagnosis of celiac disease. However, its high negative predictive value may be of use to gastrointestinal specialists in specific clinical situations.

Alternative covered services:

Clinical evaluation by physicians and appropriate standard diagnostic procedures.
**Background**

Gluten is the commonly used term for the complex of water-insoluble proteins from wheat, rye, and barley that are poorly digested in the human intestine. The immune reaction to gluten triggers an inflammatory response in the small intestine that impedes absorption of nutrients from ingested food. Gluten sensitivity disorders are common causes of chronic malabsorption in all age groups (Leonard, 2017).

Celiac disease is a chronic small intestinal immune-mediated enteropathy precipitated by exposure to dietary gluten in individuals who are genetically predisposed to specific human leukocyte antigen-DQ2 and human leukocyte antigen-DQ8 genetic markers (Leonard, 2017; Ludvigsson, 2012). Differentiating celiac disease from other disorders can be difficult because of the variety of non-specific gastrointestinal and non-gastrointestinal signs and symptoms at presentation; some patients may present with no symptoms or exhibit gluten sensitivity without celiac disease (Leonard, 2017).

Treatment for gluten sensitivity requires adherence to a gluten-free diet to allow intestinal healing and alleviate symptoms. The main hurdles for treating celiac disease are identifying which tests to use for appropriate diagnosis and avoiding unnecessary testing (Leonard, 2017). Duodenal biopsies in patients following a gluten-containing diet may be required for diagnostic confirmation and differential diagnosis of other malabsorptive disorders (Ludvigsson, 2013). Serologic and genetic tests are available for screening.

**Serologic tests** detect the presence of specific antibodies. Anti-reticulin antibodies have historically been used, but they lack optimal sensitivities and specificities for routine diagnostic use and are considered obsolete. Antiendomysial antibodies, anti-tissue transglutaminase antibodies, and deamidated anti-gliadin peptide antibodies in blood serum are used more commonly in celiac diagnosis (Ludvigsson, 2013). For each serologic test, both immunoglobulins A and G can be measured; however, immunoglobulin A measurement is the standard for diagnosing celiac disease. The newest serologic tests, deamidated gliadin peptide antibody tests, are believed to be more specific to celiac disease than tests of native peptides. Tests that are able to assay both immunoglobulin A and immunoglobulin G could be used potentially in individuals regardless of immunoglobulin A deficiency status.

**Point of care tests** are emerging as potential alternatives to laboratory-based serologic tests (Popp, 2013). Point of care tests require serum or whole blood samples. They are reportedly quick, economical, and easy to use, and can be performed on-site in the provider’s office and in primary care settings without the need for laboratory analysis. Active case finding using point of care tests may help shorten diagnostic delays, particularly in populations where diagnostic uncertainty is high.

**Genetic tests** identify a genetic predisposition to celiac disease. Human leukocyte antigen-DQ genotyping is performed by polymerase chain reaction with sequence-specific primers or hybridization of sequence-specific probes. In patients on a gluten-free diet with a positive human leukocyte antigen-
DQ, DQ2, or DQ8 result, a gluten challenge remains the gold standard for celiac disease diagnosis. A gluten challenge involves introducing a normal, gluten-rich diet under medical supervision to enable diagnostic testing (Rubio-Tapia, 2013).

Searches

Prestige Health Choice searched PubMed and the databases of:

- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality’s National Guideline Clearinghouse and other evidence-based practice centers.
- The Centers for Medicare & Medicaid Services.

We conducted searches on May 29, 2018. The search term was “celiac disease” (MeSH).

We included:

- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.
- **Guidelines based on systematic reviews**.
- **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

Findings

**Serologic testing for celiac disease:**

The results from available systematic reviews (see Appendix) indicate that immunoglobulin A-tissue transglutaminase and immunoglobulin A-endomysial antibody serologic tests show high sensitivity and specificity for diagnosing celiac disease in populations with symptoms suggestive of celiac disease (Medical Advisory Secretariat, 2010; National Institute for Health and Care Excellence, 2009). Limited evidence from studies with targeted low-prevalence populations in whom diagnostic uncertainty is higher suggests similar findings (van der Windt, 2010). Results were comparable in adults and children (Giersiepen, 2012; National Institute for Health and Care Excellence, 2009).

Additional limited evidence from these systematic reviews revealed that:

- Combination or sequential testing with immunoglobulin A-tissue transglutaminase and immunoglobulin A-endomysial antibodies does not appear to substantially improve diagnostic accuracy (Medical Advisory Secretariat, 2010; National Institute for Health and Care Excellence, 2009).
• Immunoglobulin A-tissue transglutaminase yields more false positive results in people with liver disease than in the general population (National Institute for Health and Care Excellence, 2009).
• Limited evidence suggests gliadin antibody serological tests show comparable or lower sensitivity and specificity than tissue transglutaminase and endomysial antibody tests, but these tests require further evaluation (Giersiepen, 2012; Medical Advisory Secretariat, 2010; National Institute for Health and Care Excellence, 2009).
• The presence of immunoglobulin A deficiency may affect the sensitivity of the immunoglobulin A-based serologic tests since totally or severely immunoglobulin A-deficient subjects may not produce detectable levels of immunoglobulin A antibodies (National Institute for Health and Care Excellence, 2009).
• Targeted screening with immunoglobulin A-endomysial antibodies as the preferred serologic marker would be cost effective in populations with a high prevalence of celiac disease, but additional studies are needed to establish the generalizability of the findings before implementing this screening strategy (Shamir, 2006).
• Routine screening for celiac disease in asymptomatic children with Down syndrome was not cost effective in preventing lymphoma (Swigonski, 2006).

Point of care testing:

The evidence for point of care testing for screening for celiac disease is based on two systematic reviews (Gierspiesen, 2012; National Institute for Health and Care Excellence, 2009) and one horizon scan (Purins, 2008). The evidence for point of care tests in pediatric and adult populations suggests high clinical validity for immunoglobulin A-tissue transglutaminase antibody screening. With high specificity, its clinical utility may be in ruling out celiac disease, leaving additional diagnostic testing and biopsy confirmation for those who test positive before starting a gluten-free diet. While the point of care testing may fulfill an unmet need for a simple and inexpensive case-finding biomarker for early detection and presumptive diagnosis of celiac disease, confirmatory studies are warranted for case-finding in specialized outpatient clinics and in primary care.

Human leukocyte antigen-DQ genotyping:

The clinical validity data of human leukocyte antigen-DQ genotyping for celiac disease indicate high sensitivity and negative predictive value, ranging from 92.4 percent to 100 percent and 95.4 percent to 100 percent, respectively. Human leukocyte antigen-DQ genotyping may facilitate the diagnosis of celiac disease in patients with indeterminate biopsy results. In addition, there is an increased risk for DQ2- or DQ8-positive family members (particularly first-degree relatives) of patients with confirmed celiac disease.

Despite these associations, several studies confirm that not all patients with celiac disease express DQ2 or DQ8 human leukocyte antigen molecules, and human leukocyte antigen-DQ2 or -DQ8 is present in up
to 40 percent of the general population. As such, a positive test would have no predictive value and would be insufficient to establish the diagnosis of celiac disease (National Institute for Health and Care Excellence, 2009). Therefore, the evidence does not support human leukocyte antigen-DQ genotyping as an initial test for detecting celiac disease. Patients maintained on a strict gluten-free diet without prior definitive diagnostic testing may yield negative serology and histology results. As human leukocyte antigen-DQ genotypes are not influenced by diet, a negative result may obviate the need for further work-up.

Policy updates:

A cost-effectiveness analysis applied a decision model to a screening protocol for identifying celiac disease in patients with irritable bowel syndrome with bowel habits of either diarrhea or mixed diarrhea and constipation, but not bowel habits restricted to constipation (Mohseninejad, 2013). The screening protocol consisted of serologic tissue transglutaminase testing and immunoglobulin A antibody testing followed by confirmatory endoscopy with biopsy when immunoglobulin A was less than 0.7 or greater than 0.7 with a positive tissue transglutaminase. This protocol was cost effective in the Netherlands. These results and a new guideline by the British Society of Gastroenterology are consistent with current preferred guidelines for active case-finding using serologic testing for celiac disease in patients with symptoms or conditions closely associated with celiac disease (Ludvigsson, 2014; Rubio-Tapia, 2013). This new information would not change the current policy.

In 2017, we identified two new systematic reviews/meta-analyses (Chou, 2017; Maglione, 2016), one new screening guideline from the U.S. Preventive Services Task Force (Bibbins-Domingo, 2017), and one guideline update (National Institute for Health and Care Excellence, 2015 [replaces 2009]). In symptomatic populations, strong evidence supports the high sensitivity and specificity of immunoglobulin A testing and the high specificity of immunoglobulin A-endomysial antibody testing, while moderate-quality evidence supports slightly inferior diagnostic performance of immunoglobulin A-deamidated gliadin peptide testing for detecting celiac disease (Maglione, 2016).

Based on the results of Chou et al. and Maglione et al., there remains uncertainty regarding the role of serologic testing in asymptomatic populations. The U.S. Preventive Services Task Force found insufficient evidence to recommend for or against screening for celiac disease in asymptomatic populations. The National Institute for Health and Care Excellence (2015) recommends total immunoglobulin A and immunoglobulin A-tissue transglutaminase as the preferred initial test for detecting celiac disease, followed by other serologic tests when the initial test results are abnormal or indeterminate; they reserve human leukocyte antigen-DQ2 (DQ2.2 and DQ2.5)/DQ8 testing to rule out celiac disease diagnosis in specialist settings. This new information confirms previous findings and is consistent with the current policy. Therefore, no policy changes are warranted.

In 2018, we added one meta-analysis that found tests for serum transglutaminase and endomysial antibodies had low sensitivity as surrogate markers for mucosal recovery in most patients with celiac disease on gluten-free diets (Silvester, 2017). Despite these limitations, both the North American Society
for Pediatric Gastroenterology, Hepatology, and Nutrition (Hill, 2016) and the American College of Gastroenterology (Rubio-Tapia, 2013) recommend immunoglobulin A-transglutaminase antibody testing or immunoglobulin A (or G)-deamidated anti-gliadin peptide antibody testing for monitoring patients on a gluten-free diet.

Evidence-based guidance on frequency of monitoring is absent. In adults, expert opinion suggests annual follow-up is reasonable in most cases once symptoms resolve and serology has normalized (Rubio-Tapia, 2013). Among children, achieving normal growth and development on a gluten-free diet is the main goal of monitoring. To that end, recommendations for monitoring include beginning three to six months after starting a gluten-free diet and every six months thereafter, until serology has normalized and symptoms have resolved, and then annually thereafter (Hill, 2016). Indications for monitoring and for pediatric populations were added to the medical necessity criteria.

Policy ID changed from CP# 02.07.01 to CCP.1049.

Summary of clinical evidence:

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
</tr>
</thead>
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| Bibbins-Domingo (2017) for the U.S. Preventive Services Task Force Guideline: Screening for celiac disease in asymptomatic populations | **Key points:**  
- Inadequate evidence of screening accuracy for celiac disease, the potential benefits and harms of either screening versus not screening or targeted versus universal screening, and potential benefits and harms of treatment of screen-detected celiac disease.
- Current evidence is insufficient to assess the balance of benefits and harms of screening for celiac disease in asymptomatic persons. (I statement). |
| Chou (2017) for the U.S. Preventive Services Task Force Screening for celiac disease in asymptomatic populations | **Key points:**  
- Systematic review of evidence from one prior systematic review (Maglione, 2016) and three other primary studies of randomized clinical trial, cohort, or case-control design.
- Only two studies of serologic tests for celiac disease involving 62 and 158 patients were conducted in asymptomatic populations and reported lower sensitivity (57% and 71%, respectively).
- Insufficient evidence to inform most of the key questions related to benefits and harms of screening for celiac disease in asymptomatic individuals. |
| Hill (2016) for the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition Diagnosis and treatment of gluten- | **Key points:**  
- Indicated for children with symptoms consistent with gluten-related disorders; when no other cause for symptoms can be identified; and in those with no, very minor, or less typical symptoms and at increased risk for celiac disease (e.g., first-degree relatives of an index case and people with trisomy 21, Turner syndrome, Williams syndrome, immunoglobulin A deficiency, or other autoimmune conditions).
- Immunoglobulin A-tissue transglutaminase antibody is the most cost effective and reliable initial test; consider a serum immunoglobulin A level to identify selective immunoglobulin |
<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
</tr>
</thead>
</table>
| related disorders | A deficiency.  
- Immunoglobulin A-endomysial antibody testing is less sensitive but slightly more specific and prone to false-negative and false-positive results in inexperienced hands.  
- Anti-gliadin antibody tests are poorly sensitive and specific compared with transglutaminase and endomysial tests, and are not recommended for initial diagnosis.  
- Deamidated gliadin peptide tests perform better than anti-gliadin antibody tests.  
- The deamidated gliadin peptide immunoglobulin G test has comparable specificity but lower sensitivity than the transglutaminase and endomysial immunoglobulin A tests; the deamidated gliadin peptide immunoglobulin A test is both less sensitive and less specific.  
- For a child 2 years of age, transglutaminase immunoglobulin A testing should be combined with deamidated gliadin peptide immunoglobulin G testing to improve accuracy.  
- Human leukocyte antigen testing is not recommended as an initial test.  
- Point of care tests should not replace laboratory tests.  
- Fecal tests for celiac disease-associated antibodies are not recommended. |
| Silvester (2017) Tests for serum transglutaminase and endomysial antibodies do not detect most patients with celiac disease and persistent villous atrophy on gluten-free diets | Key points:  
- Meta-analysis of 26 studies of immunoglobulin A-endomysial antibodies and immunoglobulin A-tissue transglutaminase antibodies for detection of villous atrophy while monitoring patients on gluten-free diets.  
- Results (%): Tissue transglutaminase antibody assays: sensitivity 50% (41% to 60%); specificity 83% (79% to 87%).  
- Endomysial antibody assays: sensitivity 45% (34% to 57%); specificity 91% (87% to 94%).  
- Similar results in pediatric and adult patients. |
| Maglione (2016) for the Agency for Healthcare Research and Quality Comparative accuracy and safety of diagnostic methods for celiac disease | Key points:  
- Meta-analysis of 60 studies comparing serologic testing used singly and in combination in various populations versus endoscopic duodenal biopsy, along with 13 prior systematic reviews. Majority of studies included symptomatic participants.  
- Overall quality of individual studies: Wide variation with moderate to high risk of bias.  
- Results (sensitivity; specificity; quality of evidence):  
  - Immunoglobulin A-tissue transglutaminase: 92.5%; 97.9%; high.  
  - Immunoglobulin A-endomysial antibodies: 79.0%; 99.0%; high.  
  - Immunoglobulin A-deamidated gliadin peptide: 87.8%; 94.1%; moderate.  
- Human leukocyte antigen typing can be used to rule out celiac disease with close to 100% sensitivity (high quality).  
- Insufficient evidence for:  
  - Algorithms using multiple tests.  
  - Screening asymptomatic general populations and special populations such as children and patients with type 1 diabetes, anemia, and immunoglobulin A deficiency. |
| National Institute for Health and Care Excellence (2015, update of 2009) For suspected celiac disease in young people and adults, in order of preference: | Key points:  
- Total immunoglobulin A and immunoglobulin A-tissue transglutaminase. |
<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
</tr>
</thead>
</table>
| Recognition and assessment of celiac disease | - If immunoglobulin A-tissue transglutaminase is weakly positive, test for immunoglobulin A-endomysial antibodies.  
- If immunoglobulin A is deficient, consider immunoglobulin G-endomysial antibodies, immunoglobulin G-deamidated gliadin peptide, or immunoglobulin G-tissue transglutaminase.  
  - For suspected celiac disease in children, in order of preference:  
    - Total immunoglobulin A and immunoglobulin A-tissue transglutaminase.  
    - If immunoglobulin A is deficient, consider immunoglobulin G-endomysial antibodies, immunoglobulin G-deamidated gliadin peptide, or immunoglobulin G-tissue transglutaminase.  
  - Do not use human leukocyte antigen-DQ2 (DQ2.2 and DQ2.5)/DQ8 testing in the initial diagnosis of celiac disease in non-specialist settings.  
  - Only consider human leukocyte antigen-DQ2 (DQ2.2 and DQ2.5)/DQ8 testing in the diagnosis of celiac disease in specialist settings (e.g., in children who are not having a biopsy, or in people who already have limited gluten ingestion and choose not to have a gluten challenge).  
  - Do not use serological testing alone to determine whether gluten has been excluded from the person's diet. |
| Giersiepen (2012) | Key points:  
  - Meta-analysis; immunoglobulin A-tissue transglutaminase 2 pooled sensitivity 96.4%, specificity 97.7%.  
  - Point of care tests may achieve high accuracy in the hands of experienced readers, but immunoglobulin A-tissue transglutaminase 2/endomysial antibody serologic tests were superior. |

References

Professional society guidelines/other:


Peer-reviewed references:


Purins A, Mundy L, Hiller JE. Point of care testing for Celiac disease. Adelaide: Adelaide Health Technology Assessment (AHTA); 2008. Available at:


**Centers for Medicare & Medicaid National Coverage Determinations:**

No National Coverage Determinations identified as of the writing of this policy.

**Local Coverage Determinations:**

L35000 Molecular Pathology Procedures.

L34518 Molecular Pathology Procedures for Human Leukocyte Antigen (HLA) Typing.

**Commonly submitted codes**

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>81376</td>
<td>HLA Class II typing, low resolution; HLA-DRB1/3/4/5 and DQB1</td>
<td></td>
</tr>
<tr>
<td>81383</td>
<td>HLA Class II typing, high resolution: one allele or allele group (e.g., HLA-DQB1*06:02P), each</td>
<td></td>
</tr>
<tr>
<td>82784</td>
<td>Gammaglobulin (immunoglobulin): IgA, IgD, IgG, IgM, each</td>
<td></td>
</tr>
<tr>
<td>83516</td>
<td>Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; qualitative or semiquantitative, multiple step method</td>
<td></td>
</tr>
<tr>
<td>86255</td>
<td>Fluorescent noninfectious agent antibody; screen, each antibody</td>
<td></td>
</tr>
<tr>
<td>86256</td>
<td>Fluorescent noninfectious agent antibody; titer, each antibody</td>
<td></td>
</tr>
</tbody>
</table>
ICD-10 Code | Description | Comment
--- | --- | ---
K90.0 | Celiac disease | |
Z13.2 | Encounter for screening for nutritional, metabolic, and other endocrine disorders | |

**Appendix**

**Pooled estimates of sensitivity and specificity of serological tests for celiac disease**

<table>
<thead>
<tr>
<th>Serological test</th>
<th>Systematic review</th>
<th>Sensitivity (%) (95% CI)</th>
<th>Specificity (%) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunoglobulin A anti-gliadin antibody</td>
<td>National Institute for Health and Care Excellence 2009**</td>
<td>23 – 100</td>
<td>45 – 100</td>
</tr>
<tr>
<td></td>
<td>van der Windt 2010</td>
<td>46 – 87</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Medical Advisory Secretariat 2010</td>
<td>74.9 (63.6 – 86.2)</td>
<td>90.1 – 98.7 depending on test</td>
</tr>
<tr>
<td>Immunoglobulin G anti-gliadin antibody</td>
<td>National Institute for Health and Care Excellence 2009</td>
<td>46 – 100</td>
<td>77 – 99</td>
</tr>
<tr>
<td></td>
<td>van der Windt 2010</td>
<td>25 – 93</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Medical Advisory Secretariat 2010</td>
<td>69.1 (56.0 – 82.2)</td>
<td>90.1 – 98.7 depending on test</td>
</tr>
<tr>
<td>Immunoglobulin A endomysial antibodies</td>
<td>National Institute for Health and Care Excellence 2009</td>
<td>68 – 100</td>
<td>89 – 100</td>
</tr>
<tr>
<td></td>
<td>Giersiepen 2012</td>
<td>&gt; 90</td>
<td>98.2</td>
</tr>
<tr>
<td></td>
<td>van der Windt 2010</td>
<td>90 (80 – 95) LR+ =171</td>
<td>99 (98 – 100) LR- = 0.11</td>
</tr>
<tr>
<td></td>
<td>Medical Advisory Secretariat 2010</td>
<td>85.1 (79.5 – 94.4)</td>
<td>90.1 – 98.7 depending on test</td>
</tr>
<tr>
<td>Immunoglobulin G endomysial antibodies</td>
<td>National Institute for Health and Care Excellence 2009</td>
<td>39</td>
<td>98</td>
</tr>
<tr>
<td>Immunoglobulin A tissue transglutaminase</td>
<td>National Institute for Health and Care Excellence 2009</td>
<td>38 – 100</td>
<td>25 – 100</td>
</tr>
<tr>
<td></td>
<td>Giersiepen 2012</td>
<td>≥ 90</td>
<td>≥ 90</td>
</tr>
<tr>
<td></td>
<td>van der Windt 2010</td>
<td>89 (82 – 94) LR+ = 37.7</td>
<td>98 (95 – 99) LR = 0.11</td>
</tr>
<tr>
<td></td>
<td>Medical Advisory Secretariat 2010</td>
<td>92.1 (88.0 – 96.3)</td>
<td>90.1 – 98.7 depending on test</td>
</tr>
<tr>
<td>Serological test</td>
<td>Systematic review</td>
<td>Sensitivity (%) (95% CI)</td>
<td>Specificity (%) (95% CI)</td>
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</tr>
<tr>
<td>Immunoglobulin G tissue transglutaminase</td>
<td>National Institute for Health and Care Excellence 2009</td>
<td>23 – 85</td>
<td>89 – 98</td>
</tr>
<tr>
<td></td>
<td>Medical Advisory Secretariat 2010</td>
<td>44.7 (30.3 – 59.2)</td>
<td>90.1 – 98.7 depending on test</td>
</tr>
<tr>
<td>Immunoglobulin A-deamidated gliadin peptide</td>
<td>Giersiepen 2012</td>
<td>80.7 – 95.1</td>
<td>86.3 – 93.1</td>
</tr>
<tr>
<td></td>
<td>Medical Advisory Secretariat 2010</td>
<td>89.2 (83.3 – 95.1)</td>
<td>90.1 – 98.7 depending on test</td>
</tr>
<tr>
<td>Immunoglobulin G-deamidated gliadin peptide</td>
<td>Giersiepen 2012</td>
<td>80.1 – 98.6</td>
<td>86.0 – 96.9</td>
</tr>
<tr>
<td></td>
<td>Medical Advisory Secretariat 2010</td>
<td>88.4 (82.1 – 94.6)</td>
<td>90.1 – 98.7 depending on test</td>
</tr>
</tbody>
</table>

Note: Shaded rows indicate tests with high sensitivity and specificity.
95% CI — 95 percent confidence interval.
LR — likelihood ratio.
** The National Institute for Health and Care Excellence does not recommend immunoglobulin A anti-gliadin antibody testing in the diagnosis of celiac disease.