BlueCross BlueShield of Alabama

Name of Blue Advantage Policy:

Serologic Diagnosis of Celiac Disease

Policy #: 161
Latest Review Date: June 2024
Category: Laboratory

BACKGROUND:

Blue Advantage *medical policy does not conflict with Local Coverage Determinations (LCDs), Local Medical Review Policies (LMRPs) or National Coverage Determinations (NCDs) or with coverage provisions in Medicare manuals, instructions or operational policy letters. In order to be covered by Blue Advantage the service shall be reasonable and necessary under Title XVIII of the Social Security Act, Section 1862(a)(1)(A). The service is considered reasonable and necessary if it is determined that the service is:*

1. *Safe and effective;*
2. *Not experimental or investigational*;*
3. *Appropriate, including duration and frequency that is considered appropriate for the service, in terms of whether it is:*
   - *Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;*
   - *Furnished in a setting appropriate to the patient's medical needs and condition;*
   - *Ordered and furnished by qualified personnel;*
   - *One that meets, but does not exceed, the patient's medical need; and*
   - *At least as beneficial as an existing and available medically appropriate alternative.*

Routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000, which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary by Medicare. Providers should bill* ***Original Medicare* *for covered services that are related to* ***clinical trials*** *that meet Medicare requirements (Refer to Medicare National Coverage Determinations Manual, Chapter 1, Section 310 and Medicare Claims Processing Manual Chapter 32, Sections 69.0-69.11).*

Proprietary Information of Blue Cross and Blue Shield of Alabama

POLICY:

Effective for dates of service on and after September 1, 2024:

Blue Advantage will treat **serologic measurement of IgA antibodies (i.e. antigliadin (AGA)), antiendomysial or tissue transglutaminase antibodies** as a **covered benefit** when:

- Performed to evaluate patients with signs or symptoms suggestive of celiac disease; OR
- Performed to monitor patient's adherence and response to a gluten-free diet

Blue Advantage will treat s**erologic measurement of deamidated gliadin peptide (DGP) antibodies** as a **covered benefit** in individuals with signs or symptoms suggestive of celiac disease.

Blue Advantage will treat **serologic measurement of deamidated gliadin peptide antibodies** as a **non-covered benefit** in individuals without signs or symptoms suggestive of celiac disease.

Blue Advantage will treat **screening of asymptomatic, at-risk patient groups, for celiac disease using one or more serologic IgA or IgG measures** as a **non-covered benefit.**

Blue Advantage will treat population **screening for celiac disease using one or more serologic IgA or IgG measures** as a **non-covered benefit**.

Effective for dates of service prior to September 1, 2024:

Blue Advantage will treat **serologic measurement of antigliadin, antiendomysial or tissue transglutaminase antibodies** as a **covered** benefit when:

- Performed to evaluate patients with signs or symptoms suggestive of celiac disease, **OR**
- Performed to monitor patient's adherence and response to a gluten-free diet

Blue Advantage will treat **serologic measurement of deamidated gliadin peptide antibodies** as a **non-covered benefit** and as **investigational** in patients with signs or symptoms suggestive of celiac disease.

Blue Advantage will treat **screening of asymptomatic at-risk patient groups for celiac disease** using one or more serologic IgA or IgG measures as a **non-covered** benefit and as **investigational**.

Blue Advantage will treat **population screening for celiac disease** using one or more serologic IgA or IgG measures as a **non-covered** benefit and as **investigational**.

Blue Advantage does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Advantage administers benefits based on the members' contracts and medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

DESCRIPTION OF PROCEDURE OR SERVICE:

Celiac disease is an immune disorder in which individuals are unable to tolerate gluten, a protein found in wheat, rye, and barley. Diagnosis is made based on the biopsy and histopathologic examination of the small intestine. Blood tests may be used to select individuals for biopsy and to aid in diagnosis. Celiac disease is characterized by an abnormal proximal small intestinal mucosa, and it is associated with a permanent intolerance to gluten. Both the symptoms and abnormal small intestinal mucosal morphology resolve with removal of gluten from the diet.

Because the symptoms of celiac disease are nonspecific they are often overlooked. In addition, the disease may develop at any time in life, from infancy to very old age. In adults, diarrhea is the main presenting symptom, but presenting symptoms may be entirely nonspecific, such as anemia or infertility. Celiac disease is associated with a number of other conditions, including Type 1 diabetes mellitus, rheumatoid arthritis, and primary biliary cirrhosis.

Deamidated gliadin peptide (DGP) antibody tests are the newest tests for celiac disease. Individuals are often found to have elevated levels of these antibodies if the celiac disease is untreated. The test measures levels of DGP in the blood, and if elevated it is indicative of celiac disease. The small intestine may be damaged, and malnutrition may occur in undiagnosed individuals. The test may be requested as deamidated gliadin peptide antibodies, DGP, DGP AGA, or DGP IgA and IgG. The testing method is enzyme-linked immunosorbent assay, and the specimen is serum.

KEY POINTS:

The most recent literature update was performed through June 11, 2024.

Summary of Evidence

Use of serologic tests for the diagnosis of celiac disease has the potential to reduce the need for intestinal biopsies and thus improve the efficiency of diagnosis. Evidence from systematic reviews and head-to-head comparative studies using biopsy as the gold standard is adequate to conclude that tissue transglutaminase and antiendomysial antibody tests are sufficiently accurate for identifying celiac disease in patients with signs or symptoms of the disease. These tests are appropriate for use as the diagnostic test for celiac disease and will reduce the need for intestinal biopsy without substantially lowering the accuracy of diagnosis. It should be noted, however, that the most important initial step in diagnosis is recognition of the many clinical features that can be associated with the disease.

In children younger than 2 years old, the pattern of serologies appears to be different than in older individuals. Evidence found that in children younger than 18 months, serologic measurement of antigliadin antibodies (AGA) is the most sensitive testing.
The evidence for serologic measurement of deamidated gliadin peptide antibodies (DGP) for celiac disease includes systemic reviews and meta-analyses. Of studies identified, evidence showed that some children with early celiac disease may have been missed without DGP testing. While TTG IgA is the best celiac disease test currently in children less than 2 years of age, there is evidence that the addition of DGP IgG may increase the diagnostic sensitivity. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Practice Guidelines and Position Statements
American College of Gastroenterology (ACG)
In 2023, the ACG updated its guidelines on diagnosis and management of celiac disease:

1. Patients with symptoms, signs, or laboratory evidence suggestive of malabsorption, such as chronic diarrhea with weight loss, steatorrhea, abdominal pain, and bloating, should be tested for CD.
2. Patients with symptoms, signs, or laboratory evidence for which CD is a treatable cause should be considered for testing for CD.
3. Patients with a first-degree family member who has a confirmed diagnosis of CD should be tested whether they show possible signs or symptoms or laboratory evidence of CD.
4. Consider testing of asymptomatic relatives with a first-degree family member who has a confirmed diagnosis of CD.

American Gastroenterological Association (AGA)
In 2013, the AGA issued the following position statement on the diagnosis and management of celiac disease:

Many individuals with celiac disease may have no symptoms at all. Celiac disease is usually detected by serologic testing of celiac-specific antibodies. The diagnosis is confirmed by duodenal mucosal biopsies. Both serology and biopsy should be performed on a gluten-containing diet. The treatment for celiac disease is primarily a gluten-free diet (GFD), which requires significant patient education, motivation, and follow-up. Non-responsive celiac disease occurs frequently, particularly in those diagnosed in adulthood. Persistent or recurring symptoms should lead to a review of the patient's original diagnosis to exclude alternative diagnoses, a review of the GFD to ensure there is no obvious gluten contamination, and serologic testing to confirm adherence with the GFD. In addition, evaluation for disorders associated with celiac disease that could cause persistent symptoms, such as microscopic colitis, pancreatic exocrine dysfunction, and complications of celiac disease, such as enteropathy-associated lymphoma or refractory celiac disease, should be entertained. Newer therapeutic modalities are being studied in clinical trials but are not yet approved for use in practice. Given the incomplete response of many patients to a GFD-free diet as well as the difficulty of adherence to the GFD over the long term, development of new effective therapies for symptom control and reversal of inflammation and organ damage are needed. The prevalence of celiac disease is increasing worldwide and many patients with celiac disease remain undiagnosed, highlighting the need for improved strategies in the future for the optimal detection of patients.

North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN)
In 2016, NASPGHAN issued the following guidelines on the diagnosis and treatment of celiac disease in children:

To screen patients for celiac disease (CD), measurement of the immunoglobulin A (IgA) tissue transglutaminase antibody is the preferred test. Total serum IgA level should be measured to exclude selective IgA deficiency and to avoid false-negative test results. Patients with positive serologic test results should be referred to a gastroenterologist for endoscopic small intestinal

biopsies to confirm the diagnosis. Testing for human leukocyte antigens DQ2 and DQ8 can help exclude the diagnosis. A gluten-free diet should not be started before confirming the diagnosis of CD. Serologic testing is very useful for screening patients with suspected CD. Early diagnosis is essential to prevent complications of CD.

National Institutes of Health (NIH)
According to a 2004 NIH Consensus Panel Statement on celiac disease, serological testing is the first step in pursuing a diagnosis of CD. The Consensus Statement said that the best available tests are the IgA anti-human tissue transglutaminase (TTG) and anti-endomesial IgA antibodies (EMA). According to the NIH Consensus Statement, the antigliadin IgA and IgG antibody tests are no longer routinely recommended because of their lower sensitivity and specificity.

The European Society of Pediatric Gastroenterology and Nutrition (ESPGHAN)
The European Society of Pediatric Gastroenterology and Nutrition has established criteria for definitive diagnosis of CD. In children younger than two years of age, the criteria state diagnosis would be made only when reintroduction of gluten into the diet, after the intestinal mucosa has become normal, causes the mucosa again to become abnormal, with or without symptoms. In children older than two years of age, the criteria state a second challenge with gluten is not required if the initial biopsy is positive.

According to 2020 guidelines, a no-biopsy approach is appropriate for children with TGA-IgA values ≥10 times the upper limit of normal with appropriate tests and positive endomysia antibodies (EMA-IgA) in a second serum sample.

U.S. Preventive Services Task Force Recommendations
The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for celiac disease in asymptomatic persons.

KEY WORDS:
Celiac disease, CD, celiac sprue, serologic tests, DGP, deamidated gliadin peptide, tTG, tissue transglutaminase, AGA, antigliadin antibodies, EMA, antiendomysial antibodies

APPROVED BY GOVERNING BODIES:
This testing is approved by the United States FDA.

BENEFIT APPLICATION:
Coverage is subject to member's specific benefits. Group-specific policy will supersede this policy when applicable.

CURRENT CODING:

CPT codes:

82784	Gammaglobulin; IgA, IgD, IgG, IgM, each
83516	Immunoassay for analyte other than infectious agent antibody or infectious agent antigen, qualitative or semiquantitative; multiple step method
83518	Immunoassay for analyte other than infectious agent antibody or infectious agent antigen, qualitative or semiquantitative; single step method (e.g., reagent strip)
83520	Immunoassay, analyte, quantitative; not otherwise specified
86231	Endomysial antibody (EMA), each immunoglobulin (Ig) class (Effective 01/01/22)
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 (Effective 01/01/22)
86364	Tissue transglutaminase, each immunoglobulin (Ig) class (Effective 01/01/22)
86816	HLA typing; DR/DQ, Single Antigen
88346	Immunofluorescence, per specimen; initial single antibody stain procedure
88350	each additional single antibody stain procedure (List separately in addition to code for primary procedure)

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POLICY HISTORY:

Adopted for Blue Advantage, March 2005
Available for comment May 1-June 14, 2005
Medical Policy Group, May 2007
Medical Policy Group, November 2008
Medical Policy Group, February 2009
Available for comment April 16-May 30, 2009
Medical Policy Group, September 2010
Medical Policy Group, January 2012
Medical Policy Group, September 2013
Available for comment September 19 through November 2, 2013
Medical Policy Group, January 2014
Medical Policy Group, December 2015
Medical Policy Group, June 2018
Medical Policy Group, September 2018 **(9)**: Updates to Key Points, References, added Key Words DGP, deamidated gladin peptide, TG, tissue transglutaminase, AGA, antigliadin antibodies, EMA, antiendomysial antibodies. No change to policy statement.
Medical Policy Group, June 2019
Medical Policy Group, May 2021

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Medical Policy Group, October 2021: Reviewed by consensus. No new published peer-reviewed literature available that would alter the coverage statement in this policy.
Medical Policy Group, November 2021: 2022 Annual Coding Update. Added CPT codes 86231, 86258, 86364 to the Current Coding section.
Medical Policy Group, May 2022: Reviewed by consensus. No new published peer-reviewed literature available that would alter the coverage statement in this policy.
Medical Policy Group, May 2023: Reviewed by consensus. No new published peer-reviewed literature available that would alter the coverage statement in this policy.
UM Committee, December 2023: Policy approved by UM Committee for use for Blue Advantage business.
Medical Policy Group, June 2024: Reviewed by consensus. Updates to Description, Key Points; Practice Guidelines and Position Statements, and References. Updates to Policy Statement to include criteria for serologic measurement of deamidated gliadin peptide (DGP) antibodies. Available for comment, August 1, 2024, through September 1, 2024.
UM Committee, August 2024: Annual review of policy approved by UM Committee for use for Blue Advantage business.

This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member's plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield's administration of plan contracts.