

HLA Typing for Celiac Disease

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Introduction

HLA typing for celiac disease is addressed by this guideline.

Procedures addressed

The inclusion of any procedure code in this table does not imply that the code is under management or requires prior authorization. Refer to the specific Health Plan's procedure code list for management requirements.

Procedures addressed by this guideline	Procedure codes
HLA Class II Typing- low resolution, multiple alleles	81376
HLA Class II Typing- low resolution, one allele or allele group	81377
HLA Class II Typing- high resolution, multiple alleles	81382
HLA Class II Typing- high resolution, one allele or allele group	81383

Criteria

Introduction

Requests for HLA typing for Celiac disease are reviewed using these criteria.

Criteria

Testing is medically necessary in individuals who meet the following criteria.

- Celiac disease is in the differential diagnosis based on one of the following:
 - Negative celiac disease-specific antibodies and mild infiltrative changes in small-bowel specimens, or
 - Mild infiltrative changes in small-bowel specimens, or
 - First-degree relatives of an individual with confirmed celiac disease, or
 - Individuals with autoimmune and non-autoimmune conditions known to be associated with celiac disease, such as

- Type 1 Diabetes
- Down syndrome
- Turner syndrome
- Williams syndrome

No more than 2 units per lifetime are medically necessary.

Billing and Reimbursement

Introduction

This section outlines the billing requirements for tests addressed in this guideline. These requirements will be enforced during the case review process whenever appropriate. Examples of requirements may include specific coding scenarios, limits on allowable test combinations or frequency and/or information that must be provided on a claim for automated processing. Any claims submitted without the necessary information to allow for automated processing (e.g. ICD code, place of service, etc.) will not be reimbursable as billed. Any claim may require submission of medical records for post service review.

Testing is reimbursable when billed with an ICD code from *Table: Celiac Disease Testing Indications*.

ICD Codes

ICD codes used for automated claims processing for this guideline.

Table: Celiac Disease Testing Indications

Codes and descriptions

Code or Range	Description
D50.8	Other iron deficiency anemias
D50.9	Iron deficiency anemia, unspecified
D51.8	Other vitamin B12 deficiency anemias
D51.9	Vitamin B12 deficiency anemia, unspecified
D52.9	Folate deficiency anemia, unspecified
D80.1	Hypogammaglobulinemia
D80.2	Selective IgA deficiency
D83.9	Common variable immunodeficiency, unspecified

Code or Range	Description
E03.9	Hypothyroidism, unspecified
E10.X	Type 1 Diabetes Mellitus
E61.X	Deficiency of other nutrient elements
E83.X	Disorders of mineral metabolism
E88.A	Wasting disease (syndrome) due to underlying condition
G62.9	Polyneuropathy, unspecified
K03.X	Other diseases of hard tissues of teeth
K12.0	Recurrent oral aphthae
K13.0	Angular cheilosis
K14.0	Glossitis
K21.X	Gastro-esophageal reflux disease
K52.9	Noninfective gastroenteritis and colitis, unspecified
K58.X	Irritable bowel syndrome
K59.00-K59.09	Constipation
K76.0	Fatty liver, not elsewhere classified
K90.0	Celiac Disease
K90.9	Intestinal malabsorption, unspecified
L13.0	Dermatitis herpetiformis
M06.4	Inflammatory polyarthropathy
M07.6	Enteropathic arthropathies
M13.0	Polyarthritis, unspecified
M13.1-M13.179	Monoarthritis, not elsewhere classified
M13.80-M13.89	Other specified arthritis
M19.90	Arthritis
M25.50-M25.579	Joint pain
M81.0	Osteoporosis
M85.8	Osteopenia
M85.80	Bone pain
P92.6	Failure to thrive in newborn
Q82.8	Follicular keratosis (keratosis pilaris)

Code or Range	Description
Q90.0-Q90.9	Down Syndrome
Q93.82	Williams syndrome
Q96.9	Turner's syndrome, unspecified
R10.0-R10.9	Abdominal and pelvic pain
R11.0-R11.2	Nausea and vomiting
R14.0-R14.3	Flatulence and related conditions
R19.7	Diarrhea, unspecified
R60	Edema, not elsewhere classified
R62.52	Short stature, child
R63.4	Abnormal weight loss
R63.6	Underweight
R68.3	Clubbing of fingers
R74.X	Abnormal serum enzyme levels
Z83.79	Family history of other diseases of the digestive system

What is Celiac disease?

Definition

Celiac disease is an immune-mediated disorder that mainly affects the digestive tract.¹⁻⁴

Symptoms

Symptoms include diarrhea, constipation, vomiting, abdominal pain and bloating, growth problems, iron deficiency anemia, osteoporosis, and other complications of malabsorption.¹⁻⁴

Prevalence

Celiac disease affects infants, children, and adults and can present at any age. It affects about 1 in every 100 individuals in the U.S.^{2,3}

Cause

Celiac disease is caused by multiple factors, including environmental trigger in a genetically predisposed individual, upon exposure to dietary gluten, which is a protein molecule found in wheat, barley and rye.¹⁻⁴

Diagnosis

An initial diagnosis of celiac disease is highly suspected based on serologic testing and is confirmed by finding characteristic changes on intestinal biopsy. Intestinal biopsy remains the gold standard for making a diagnosis of celiac disease.¹⁻⁴

Increased risk

Individuals with certain medical conditions and relatives of individuals with celiac disease are known to have an increased risk of developing the condition.^{2,3}

Test information

Introduction

Two HLA haplotypes are associated with celiac disease: HLA-DQ2 and HLA-DQ8, and are determined by molecular testing of the genes HLA-DQA1 and HLA-DQB1. These haplotypes are present in about 30-40% of the general population, but more than 99% of patients with celiac disease have one or more of these variants¹. If an individual suspected of having celiac disease is found not to have one of these markers, the diagnosis can be essentially excluded.²⁻⁴

Guidelines and evidence

Introduction

This section includes relevant guidelines and evidence pertaining to Celiac disease testing.

Guidelines

Consensus-based guidelines from the American Gastroenterological Association (2019), the National Institutes of Health (2005), North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (2005) and the 2023 American College of Gastroenterology Practice Guidelines stated that HLA typing for celiac disease should be used as outlined in this table.²⁻⁵

Test type	Use	Level of recommendation
Human leukocyte antigen DQ2/DQ8 testing	Do not use routinely in the initial diagnosis of Celiac disease	Strong recommendation, moderate level of evidence
Human leukocyte antigen DQ2/DQ8 genotyping testing	Use to effectively rule out the disease in selected clinical situations	

The World Gastroenterology Organisation Global Guidelines on Celiac disease (2016) stated that for first degree relatives of individuals with celiac disease, no further work-up is necessary in those who test negative for HLA-DQ2/8.⁶

References

Introduction

These references are cited in this guideline.

1. Snyder C, Young D, Green P, Taylor A. (Updated January 21, 2019). Celiac disease. In: GeneReviews at GeneTests: Medical Genetics Information Resource (database online). Copyright University of Washington, Seattle. 1993-2021. Available at: <http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=celiac>
2. Husby S, Murray JA, and Katzka DA. AGA clinical practice update on diagnosis and monitoring of celiac disease: changing utility of serology and histologic measures: expert review. *Gastroenterology*. 2019;156(4):885-889.
3. National Institutes of Health. NIH Consensus Development Conference Statement on Celiac Disease, June 28-30, 2004. *Gastroenterology*. 2005;128:S1-S9.
4. North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHN). Clinical guideline for the diagnosis and treatment of celiac disease in children. *J Pediatr Gastroenterol Nutr*. 2005;40:1-19.
5. Rubio-Tapia A, Hill ID, Semrad C, et al. American College of Gastroenterology guidelines update: Diagnosis and management of celiac disease. *Am J Gastroenterol*. 2023;118(1):59-76. doi: 10.14309/ajg.0000000000002075 Bai JO, Ciacci C, Corazza GR, et al.
6. World Gastroenterology Organisation Global Guidelines:Celiac Disease. (July 2016). Available at: <http://www.worldgastroenterology.org/guidelines/global-guidelines/celiac-disease/celiac-disease-english>