



# GENETIC TESTING: GASTROENTEROLOGY (NON-CANCEROUS) DISORDERS (REQUIRES PREAUTHORIZATION)

V.67

## V.67 GENETIC TESTING: GASTROENTEROLOGY (NON-CANCEROUS) DISORDERS (REQUIRES PREAUTHORIZATION)

### DESCRIPTION

Genetic Testing for gastroenterologic (non-cancerous) disorders may be used to confirm a diagnosis in a patient who has signs and/or symptoms of a specific gastroenterologic disorder. Confirming the diagnosis may alter aspects of management and may eliminate the need or further diagnostic workup. This policy addresses genetic testing for common gastroenterologic (non-cancerous) conditions.

### Dates

Original Effective

**03-09-2021**

Last Review

**08-07-2024**

Next Review

**08-11-2025**

### RELATED POLICIES

This policy document provides coverage criteria for Genetic Testing for Gastroenterologic Conditions (Non-Cancerous). Please refer to:

***Genetic Testing: Hereditary Cancer Susceptibility Syndromes***  
for coverage criteria related to germline testing for hereditary cancer syndromes, including Lynch/HNPCC syndrome.

***Genetic Testing: Prenatal and Preconception Carrier Screening*** for coverage criteria related to carrier screening in the prenatal, preimplantation, and preconception setting.



to diagnose genetic conditions following amniocentesis, chorionic villus sampling or pregnancy loss.

***Genetic Testing: Multisystem Inherited Disorders, Intellectual Disability, and Developmental Delay*** for coverage criteria related to diagnostic genetic testing for conditions affecting multiple organ systems.

***Genetic Testing: Metabolic, Endocrine, and Mitochondrial Disorders*** for coverage criteria related to genetic testing for MTHFR.

***Genetic Testing: General Approach to Genetic Testing*** for coverage criteria related to genetic testing for any non-cancerous GI disorders that is not specifically discussed in this or another non-general policy.

## REFERENCE TABLE

The tests, associated laboratories, CPT codes, and ICD codes contained within this document serve only as examples to help users navigate claims and corresponding coverage criteria; as such, they are not comprehensive and are not a guarantee of coverage or non-coverage. Please see the [Concert Platform](#) for a comprehensive list of registered tests.

<u>Coverage Criteria Sections</u>	Example Tests (Labs)	Common CPT Codes	Common ICD Codes	<u>Ref</u>
<u>Celiac Disease</u>				
<u>HLA-DQ Genotyping Analysis</u>	Celiac HLA DQ Association (Labcorp)	81375, 81376, 81377,	K90.0, R10.0- R10.13, R10.3- R10.829, R10.84- R10.9	4, 5, 6
	HLA Typing for Celiac Disease (Quest Diagnostics)	81382, 81383		
<u>Hereditary Hemochromatosis</u>				
<u>HFE C282Y and H63D Genotyping</u>	Hereditary Hemochromatosis DNA Mutation Analysis (Quest Diagnostics)	81256	E83.110, E83.118, E83.119, R79.0, E83.19, R16.0	1, 7, 12
	HFE Targeted Variant - Single Test (GeneDx)			



<a href="#">Multigene Panel</a>		81404, 81405, 81479		13, 14
<b><u>Inflammatory Bowel Disease</u></b>				
<a href="#">Inflammatory Bowel Disease / Crohn's Disease Diagnostic Algorithmic Tests</a>	Prometheus IBD sgi Diagnostic (Prometheus Laboratories)	81479, 82397, 83520, 86140, 88346, 88350	K50-K52	8
<a href="#">Inflammatory Bowel Disease / Crohn's Disease Prognostic Algorithmic Tests</a>	Prometheus Crohn's Prognostic (Prometheus Laboratories)  PredictSURE IBD (KSL Diagnostics)	81401, 83520, 88346, 88350  0203U	K50-K52	9
<a href="#">Hereditary Inflammatory Bowel Disease / Crohn's Disease Panel Tests</a>	Monogenic Inflammatory Bowel Disease Panel (Invitae)  Very Early Onset Inflammatory Bowel (VEO-IBD) Panel (Children's Hospital of Philadelphia - Division of Genomic Diagnostics)	81479, 81321, 81406, 81407	K50-K52	10, 11
<b><u>Non-invasive Liver Fibrosis Serum Tests</u></b>				
<a href="#">Non-invasive Liver Fibrosis Serum Tests</a>	ASH FibroSURE (LabCorp) NASH FibroSURE (LabCorp)  FIB-4 Index Panel with Reflex to Enhanced Liver Fibrosis (ELF) Score (Quest Diagnostics)  Enhanced Liver Fibrosis (ELF) Test (Siemens Health Care Diagnostics)	0002M, 0003M  84450, 84460, 85049  81517	K76.0, R74.8, R94.5, R79.89, I10	15, 16, 17, 18
<b><u>Test Specific Not Covered Gastroenterologic Disorders Tests</u></b>				
Test Specific Not Covered Gastroenterologic Disorders Tests	EsoGuard (Lucid Diagnostics)	0114U	K22.7, K74, K75,	16, 17, 18



## POLICY

### CELIAC DISEASE

#### *HLA-DQ* Genotyping Analysis

- I. *HLA-DQA1* and *HLA-DQB1* genotyping analysis (81375, 81376, 81377, 81382, 81383) to rule out celiac disease (CD) is considered **medically necessary** when:
  - A. The member is being evaluated for celiac disease, **AND**
    1. Had an inconclusive serology (antibody) result, **OR**
    2. Had an inconclusive histology (biopsy) result, **OR**
    3. Started a gluten-free diet before evaluation for celiac disease, **AND**
  - B. *HLA-DQA1* and *HLA-DQB1* genotyping analysis has not been previously performed.
- II. *HLA-DQA1* and *HLA-DQB1* genotyping analysis (81375, 81376, 81377, 81382, 81383) to rule out celiac disease is considered **investigational** for all other indications.

### HEREDITARY HEMOCHROMATOSIS

#### *HFE* C282Y and H63D Genotyping

- I. *HFE* C282Y and H63D genotyping (81256) to establish a diagnosis of hereditary hemochromatosis is considered **medically necessary** when:
  - A. The member has abnormal serum iron indices (e.g., elevated serum transferrin-iron saturation and/or elevated serum ferritin concentration, indicating iron overload), **OR**
  - B. The member has a first-degree relative with a diagnosis of hereditary hemochromatosis.
- II. *HFE* C282Y and H63D genotyping (81256) to establish a diagnosis of hereditary hemochromatosis is considered **investigational** for all other indications, including general population screening for hereditary hemochromatosis.

### HEREDITARY PANCREATITIS

#### Hereditary Pancreatitis Multigene Panel

- I. Hereditary pancreatitis multigene panel analysis (81222, 81223, 81404, 81405, 81479) to establish a diagnosis of hereditary pancreatitis is considered **medically necessary** when:



1. Unexplained episode of acute pancreatitis in childhood (18 years or younger), **OR**
2. Recurrent (two or more separate, documented) acute attacks of pancreatitis for which there is no explanation (i.e., anatomical anomalies, ampullary or main pancreatic strictures, trauma, viral infection, gallstones, alcohol, drugs, hyperlipidemia, etc.), **OR**
3. Chronic pancreatitis of unknown cause, particularly with onset before age 35 years without a history of heavy alcohol use, **OR**
4. At least one close relative with recurrent acute pancreatitis, chronic pancreatitis of unknown cause, or childhood pancreatitis of unknown cause, **AND**

C. The panel includes, at a minimum, the following genes: *PRSS1*, *SPINK*, *CFTR*, and *CTRC*.

II. Hereditary pancreatitis multigene panel analysis (81222, 81223, 81404, 81405, 81479) to establish a diagnosis of hereditary pancreatitis is considered **investigational** for all other indications.

## INFLAMMATORY BOWEL DISEASE

### Inflammatory Bowel Disease / Crohn's Disease Diagnostic

#### Algorithmic Tests

- I. Inflammatory bowel disease diagnostic algorithmic tests (81479, 82397, 83520, 86140, 88346, 88350) are considered **investigational**.

### Inflammatory Bowel Disease / Crohn's Disease Prognostic

#### Algorithmic Tests

- I. Inflammatory bowel disease prognostic algorithmic tests (81401, 83520, 88346, 88350) are considered **investigational**.

### Hereditary Inflammatory Bowel Disease / Crohn's Disease Panel Tests



A. The member was diagnosed with infantile-onset inflammatory bowel disease (Infantile-IBD) before age 2 years, **OR**

B. The member was diagnosed with very early onset inflammatory bowel disease (VEO-IBD) before age 6 years,  
**AND**

1. At least one of the following:

a) The member has congenital multiple intestinal atresias, **OR**

b) The member has congenital diarrhea,  
**OR**

c) The member has a diagnosis of malignancy under age 25, **OR**

d) The member has features of an inborn error of immunity such as susceptibility to infections, **OR**

e) The member has complex autoimmune features, **OR**

f) The member has a close relative meeting any of the above criteria, **OR**

2. The member is undergoing stem cell transplant, **OR**

3. The member has a history of multiple intestinal resections.

I. Genetic testing for inflammatory bowel disease (81479, 81321, 81406, 81407), including Crohn's disease, via a multigene panel is considered **investigational** for all other indications.

## NON-INVASIVE LIVER FIBROSIS SERUM TESTS

### Non-Invasive Liver Fibrosis Serum Tests

I. Non-invasive liver fibrosis serum tests (0002M, 0003M, 84450, 84460, 85049) to rule out liver fibrosis are considered **medically necessary** when:

A. The member has one of the following:

1. Nonalcoholic fatty liver disease (NAFLD), also known as metabolic dysfunction-associated steatotic liver disease (MASLD), **OR**

2. Nonalcoholic steatohepatitis (NASH), **OR**

3. Type 2 diabetes, **OR**



- B. The member had previous fibrosis-4 index (FIB-4) testing with a score of greater than 1.3.
- II. Non-invasive liver fibrosis serum tests (0002M, 0003M, 84450, 84460, 85049) to rule out liver fibrosis are considered **investigational** for all other indications.

## DEFINITIONS

1. **Close relatives** include first, second, and third degree blood relatives on the same side of the family:

- a. **First-degree relatives** are parents, siblings, and children
- b. **Second-degree relatives** are grandparents, aunts, uncles, nieces, nephews, grandchildren, and half siblings
- c. **Third-degree relatives** are great grandparents, great aunts, great uncles, great grandchildren, and first cousins

2. **Infantile-onset inflammatory bowel disease (Infantile-IBD)** is defined as clinical manifestations and/or receiving the diagnosis when younger than 2 years of age. (Ouahed, et al)

3. **Very early onset inflammatory bowel disease (VEO-IBD)** is defined as clinical manifestations and/or receiving the diagnosis when younger than 6 years of age. (Ouahed, et al)

4. **Fibrosis-4 index(FIB-4)** is a blood test that measures the probability of advanced liver fibrosis based on AST, ALT, platelets, and age.

## PRACTICE GUIDELINES AND POSITION STATEMENTS

### **HLA-DQ Genotyping Analysis**

*American College of Gastroenterology (ACG)*

The guidelines from the American College of Gastroenterology (2023) addressing the diagnosis and management of celiac disease (CD)



negative, celiac disease is ruled out. HLA testing is also central to the approach to CD testing for individuals who have already started a GFD (gluten free diet) before evaluation; in the presence of a CD-compatible haplotype, a gluten challenge can be offered. (p. 63-64)

#### *American Gastroenterological Association*

A clinical practice update on diagnosis and monitoring of celiac disease (2019) states that HLA testing has value in its negative predictive value to rule out CD in patients who are seronegative but have histologic changes or did not have serology at the time of diagnosis. HLA testing may be reserved for second line evaluation of patients with an equivocal diagnosis (inconclusive serology, histology or prior gluten free diet).

#### *U.S. Preventive Services Task Force*

The US Preventive Service Task Force (2017) released guidelines on screening adults and children for CD. These guidelines reviewed the use of tTG IgA testing followed by an intestinal biopsy to screen asymptomatic patients. Genotype testing was not discussed. The overall conclusion of this review was that the current balance of evidence was insufficient to assess benefits and harms resulting from screening for CD. (p. 1252)

### **HFE C282Y and H63D Genotyping**

#### *European Molecular Quality Network (EMQN)*

In 2015, the EMQN developed best practice guidelines to guide criteria and strategies for molecular genetic testing for hereditary hemochromatosis (HH).

The article includes guidelines, which state the following evidence-based recommendations for *HFE* testing strategies:

- “Laboratories providing testing for HFE-associated HH should test for p.C282Y (1A)
- According to local practice, p.H63D can be considered an optional complementary test that can be offered sequentially or simultaneously to p.C282Y testing (2C)
- Population screening for the p.C282Y variant is not currently recommended (1B)
- It is considered to be good practice to confirm elevated TS [transferrin saturation] before HFE genetic diagnosis testing





In 2019, practice guidelines from the ACG made the following statement on genetic testing for hereditary hemochromatosis (HH):

- “We recommend that family members, particularly first-degree relatives, of patients diagnosed with HH should be screened for HH (strong recommendation, moderate quality of evidence).” (p. 1203)
- “Selective screening of first-degree relatives of patients affected with type1 HH is suggested. Studies of patients with HH and their families have demonstrated that most homozygous relatives of probands demonstrate biochemical and clinical expression of the disease, not only due to the presence of the genetic mutation but also shared environmental factors that may increase the penetrance of the disease.” (p. 1206)
- “We recommend that individuals with the H63D or S65C mutation in the absence of C282Y mutation should be counseled that they are not at increased risk of iron overload (conditional recommendation, very low quality of evidence).” (p. 1208)

Additionally, the ACG published a suggested algorithm for diagnosis and treatment in their 2019 practice guidelines. This algorithm includes evaluating a patient's serum transferrin iron saturation (TS) and serum ferritin (SF), and indicates *HFE* genotyping if TS is 45% or greater, and/or SF is elevated. (p. 1212)

#### *GeneReviews-HFE Hemochromatosis*

GeneReviews is an expert-authored review of current literature on a genetic disease, and goes through a rigorous editing and peer review process before being published online.

Per GeneReviews, “*HFE* hemochromatosis should be suspected in individuals with...clinical signs of advanced iron overload, biochemical evidence of hemochromatosis, and/or family history of *HFE* hemochromatosis.”

#### **Hereditary Pancreatitis Multigene Panel**

##### *American College of Gastroenterology*

In 2013, the American College of Gastroenterology issued guidelines on management of acute pancreatitis and included the following statement:



low quality of evidence).” (p. 1402)

In 2020, the American College of Gastroenterology Clinical Guideline: Chronic pancreatitis (CP) recommended genetic testing in patients with clinical evidence of a pancreatitis-associated disorder or possible CP in which the etiology is unclear, especially in younger patients. At minimum, patients with idiopathic CP should be evaluated for *PRSS1*, *SPINK1*, *CFTR*, and *CTRC* gene mutation analysis, although more extended panels with over a dozen susceptibility and modifier genes, hyper- triglyceridemia genes, and pharmacogenetics are available. (p. 325 and 330)

#### *American Pancreatic Association*

In 2014, the American Pancreatic Association published Practice Guidelines in Chronic Pancreatitis: Evidence-Based Report on Diagnostic Guidelines. A classification guideline for the etiology of chronic pancreatitis (CP) includes genetic mutations in *PRSS1*, *CFTR*, *SPINK1*, and others. (p. 7)

#### *GeneReviews - Pancreatitis Overview*

GeneReviews is an expert-authored review of current literature on a genetic disease, and goes through a rigorous editing and peer review process before being published online.

According to GeneReviews, the evaluation of an at-risk individual for chronic pancreatitis should begin with the first episode of acute pancreatitis, after common causes such as gallstone, trauma, hypertriglyceridemia or hypercalcemia have been ruled out.

Molecular genetic testing for hereditary pancreatitis is indicated in a proband with pancreatitis and at least one of the following:

- An unexplained documented episode of acute pancreatitis in childhood
- Recurrent acute attacks of pancreatitis of unknown cause
- Chronic pancreatitis of unknown cause, particularly with onset before age 35 years without a history of heavy alcohol use (>5 drinks per day).
- A history of at least one relative with recurrent acute pancreatitis, chronic pancreatitis of unknown cause, or childhood pancreatitis of unknown cause



#### Algorithmic Tests

##### *Concert - Evidence Review for Coverage Determination (Published 07/1/2024)*

There are several professional society guidelines that address appropriate diagnostic tools for IBD. These include the 2018 statement by the American College of Gastroenterology (ACG) on management of adult Crohn's Disease, the 2019 guideline on Ulcerative Colitis in Adults by ACG, and the 2017 guideline by the European Crohn's and Colitis Organization (ECCO) on Diagnosis and Management of Ulcerative Colitis. The ACG Crohn's Disease and Ulcerative Colitis guidelines indicated that routine serologic testing for either disease is not recommended, with the 2019 guideline stating "we recommend against serologic antibody testing to establish or rule out a diagnosis of UC (strong recommendation, very low quality of evidence)." (p. 486 [2018 guideline], p. 385 [2019 guideline]) The ECCO evidence review and consensus concluded that the serological biomarker use of pANCA and ASCA for diagnosis and therapeutic decisions in ulcerative colitis is not clinically justified. (p. 653)

This review focused on identification of peer-reviewed, published evidence of the clinical validity and utility of Prometheus IBD sgi Diagnostic from May 1, 2023 through May 2, 2024. A PubMed search was performed. Search terms included: Prometheus ibd sgi Diagnostic, inflammatory bowel disease, systematic review, meta-analysis, and guidelines. No new literature was identified to include in the evidence review.

At the present time, IBD Crohn's Diagnostic Algorithmic tests such as Prometheus IBD sgi Diagnostic, have **INSUFFICIENT EVIDENCE** in peer-reviewed publications to effectively result in improved health outcomes compared to the current standard of care.

#### **Inflammatory Bowel Disease / Crohn's Disease Prognostic Algorithmic Tests**

##### *Concert Evidence Review for Coverage Determination (Published 7/1/2024)*

The 2018 statement by the American College of Gastroenterology (ACG) on management of adult Crohn's Disease states that certain genetic markers are associated with different phenotypic expressions in Crohn's disease but testing remains a research tool at this time." (p.



This review focused on peer-reviewed, published evidence of the clinical utility and validity of Prometheus Crohn's Prognostic test from May 1, 2023 through May 8, 2024. A PubMed search was performed. Search terms included: Crohn's disease, prognostic, biomarker, inflammatory bowel disease, guidelines, genetic testing, Prometheus Crohn's, Prometheus, clinical validity, biomarkers in ulcerative colitis/Crohn's disease.

**No new literature was identified to include in the evidence review.**

At the present time, Prometheus Crohn's Prognostic test has **INSUFFICIENT EVIDENCE** in peer-reviewed publications to effectively result in improved health outcomes compared to the current standard of care.

**Hereditary Inflammatory Bowel Disease / Crohn's Disease Panel Tests**

*UpToDate (Higuchi LM and Bousvaros A, 2022)*

The following clinical features suggest the possibility of monogenic IBD:

- Onset under age 6, especially under age 2
- Family history of IBD and/or immunodeficiency in multiple relatives, especially in males or in families with consanguinity
- Recurrent infections or unexplained fever
- Associated autoimmune features (e.g., arthritis, primary sclerosing cholangitis, anemia, or endocrine dysfunction)
- Very severe IBD, complex fistulizing disease and/or resistance to conventional IBD treatment
- Symptoms or signs of hemophagocytic lymphohistiocytosis (hepatomegaly, fever, cytopenias, high ferritin)
- Current or past history of cancer in the patient
- Endoscopic biopsies showing tissue eosinophilia and villous flattening without suggestion of celiac disease

Infants or young children presenting with these features should be referred to an immunologist for careful consideration of and evaluation for monogenic IBD. Testing may include panel, exome, or genome sequencing, and is recommended for all children under age 2, as well



*British Society of Gastroenterology and British Society of Paediatric Gastroenterology, Hepatology and Nutrition*

This joint guideline (2023) states that monogenic causes of IBD should be considered in patients with IBD since optimal care pathways and treatment may differ from that of classical IBD (high quality evidence, strong recommendation). (p.18) In monogenic IBD, panel testing is favored due to the rarity of the disorders and heterogeneous phenotypes.

Clinicians should consider genomic testing in all patients with infantile onset IBD and in very-early-onset (defined as under age 6) IBD, particularly in the presence of one or more additional testing criteria (see below) (high quality evidence, strong recommendation). (p.25) Genomic testing should only be offered in exceptional circumstances to patients with onset after age 6 (moderate quality evidence, conditional recommendation).

The following testing criteria are proposed:

- Age of IBD onset: younger than 2 years or younger than 6 years particularly when additional criteria are observed
- Infection susceptibility (eg, due to recurrent sinopulmonary infections, systemic infections, meningitis, gastrointestinal infections, or cutaneous infections) in the presence of abnormal laboratory tests (eg, congenital lymphopenia or neutropenia, or combined immunoglobulin concentration abnormalities) meeting diagnostic criteria of an inborn error of immunity (ie, primary immunodeficiency)
- Inflammatory features indicative for an inborn error of immunity, such as complex autoimmune features (especially features of IPEX syndrome in the paediatric population or severe multiorgan autoimmune disease in the adult population) or haemophagocytic lymphohistiocytosis
- Congenital multiple intestinal atresias or congenital diarrhea
- Early-onset malignancy (age <25 years)
- Family history of suspected monogenic IBD (criteria 1–5)
- In advance of interventions or therapies with irreversible consequences and high risk for adverse



resections and associated risk of short bowel syndrome, and total parenteral nutrition requirement.  
(p. 8)

### **Non-invasive Liver Fibrosis Serum Tests**

*Wattacheril, et al*

The American Gastroenterological Association (AGA) released a clinical practice update expert review (2023) regarding the role of noninvasive biomarkers in the evaluation and management of nonalcoholic fatty liver disease. They produced several best practice advice statements including the following:

- “Non-invasive tests can be used for risk stratification in the diagnostic evaluation of patients with nonalcoholic fatty liver disease (NAFLD);
- Liver biopsy should be considered for patients with NIT results that are indeterminate or discordant; conflict with other clinical, laboratory, or radiologic findings; or when alternative etiologies for liver disease are suspected.
- A combination of 2 or more NITs combining serum biomarkers and/or imaging-based biomarkers is preferred for staging and risk stratification of patients with NAFLD whose Fibrosis 4 Index score is >1.3.” (p. 1080)

Although FIB-4 score does not outperform other proprietary fibrosis biomarkers (eg, FibroTest/FibroSure [eviCore Healthcare], FIBROSpect NASH [Prometheus Laboratories], Hepamet Fibrosis Score, a Pro-C3 based score [ADAPT], FibroMeter [ARUP Laboratories], and Hepascore), FIB-4 is recommended as a firstline assessment for practitioners based on its simplicity and low cost. (p. 1081)

*Canivet, et al*

A review of screening for liver fibrosis in the general population (2022) stated that diagnostic studies using liver biopsy as a reference have demonstrated good rule-out sensitivity (80–90%) and good rule-in specificity (90–95%) of these NITs [noninvasive tests] for the diagnosis of advanced liver fibrosis in chronic liver diseases. Because these specialized blood tests include more expensive blood markers, they are best reserved for second-line evaluations of liver fibrosis, as recently proposed. (p. 7)



*Cusi, et al*

The American Association of Clinical Endocrinology (2022) produced a guideline that includes 34 evidence-based clinical practice recommendations for the diagnosis and management of persons with NAFLD and/or NASH in primary care and endocrinology clinical settings. They state that the following:

- “In persons at high risk of nonalcoholic fatty liver disease NAFLD (eg, type 2 diabetes mellitus, obesity, and metabolic syndrome), abdominal ultrasound is not required to diagnose hepatic steatosis, and it is reasonable to move directly to risk stratification after ruling out the secondary causes of liver disease.” (p. 536)
- “Recommendation 2.1.1. Clinicians should consider persons with obesity and/or features of MetS, those with prediabetes or T2D, and those with hepatic steatosis on any imaging study and/or persistently elevated plasma aminotransferase levels (over 6 months) to be “high risk” and screen for NAFLD and advanced fibrosis.” (p. 536)
- “Recommendation 2.2.1. Clinicians should use liver fibrosis prediction calculations to assess the risk of NAFLD with liver fibrosis. The preferred noninvasive initial test is the fibrosis-4 index (FIB-4).” (p. 537)
- “Recommendation 2.4.3: Clinicians should further risk stratify persons with T2D or T1D with cardiometabolic risk factors and/or elevated plasma aminotransferase levels (>30 U/L) using the FIB-4 elastography, and/or ELF test.” (p. 538)
- “In high-risk populations (i.e., those with obesity and T2D), pharmacologic therapy to treat obesity or diabetes may also be considered in the presence of elevated plasma aminotransferase levels and/or FIB-4 scores of >1.3 and confirmatory imaging (ie, TE and MRE) or proprietary fibrosis biomarkers, such as the ELF test, when suggestive of clinically significant liver fibrosis, if imaging is not available.” (p. 544)

*Rinella, et al*

The American Association for the Study of Liver Diseases issued a practice guideline (2023) for the clinical assessment and management of non alcoholic fatty liver disease. They recommend targeted



identify and manage those with clinically significant fibrosis (stage 2 or higher). In the primary care setting, emphasis is on excluding advanced fibrosis using a test with a high negative predictive value such as FIB-4. (p. 1806-1807)

## Quick Code Search

Use this feature to find out if a procedure and diagnosis code pair will be approved, denied or held for review. Simply put in the procedure code, then the diagnosis code, then click "Add Code Pair". If the codes are listed in this policy, we will help you by showing a dropdown to help you.

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### Diagnosis

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## CODES

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## REFERENCES





Gastroenterol. 2019 Dec;114(12):1927]. *Am J Gastroenterol*. 2019;114(8):1202-1218. doi:10.14309/ajg.0000000000000315

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## 2014

Conwell DL, Lee LS, Yadav D, et al. American Pancreatic Association Practice Guidelines in Chronic Pancreatitis: evidence-based report on diagnostic guidelines. *Pancreas*. 2014;43(8):1143-1162. doi:10.1097/MPA.0000000000000237

---

## 2013

Tenner S, Baillie J, DeWitt J, Vege SS; American College of Gastroenterology. American College of Gastroenterology guideline: management of acute pancreatitis [published correction appears in *Am J Gastroenterol*. 2014 Feb;109(2):302]. *Am J Gastroenterol*. 2013;108(9):1400-1416. doi:10.1038/ajg.2013.218

---

## 2013

Rubio-Tapia A, Hill ID, Kelly CP, Calderwood AH, Murray JA; American College of Gastroenterology. ACG clinical guidelines: diagnosis and management of celiac disease. *Am J Gastroenterol*. 2013;108(5):656-677. doi:10.1038/ajg.2013.79

---

## 2017

US Preventive Services Task Force, Bibbins-Domingo K, Grossman DC, et al. Screening for Celiac Disease: US Preventive Services Task Force Recommendation Statement. *JAMA*. 2017;317(12):1252-1257. doi:10.1001/jama.2017.1462

---

## 2000

Barton JC, Edwards CQ. HFE Hemochromatosis. 2000 Apr 3 [Updated 2018 Dec 6]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. *GeneReviews®* [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2023. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK1440/>

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## 2024

Concert Evidence Review for Coverage Determination. Inflammatory Bowel Disease/Crohn's Diagnostic Algorithmic Tests. Published 7/1/2024.

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## 2024

**2021**

Higuchi LM and Bousvaros A. Clinical presentation and diagnosis of inflammatory bowel disease in children. In Heyman MB, ed. UpToDate. UpToDate, 2021. Accessed November 29, 2021.

<https://www.uptodate.com/contents/clinical-presentation-and-diagnosis-of-inflammatory-bowel-disease-in-children>

**2016**

Porto G, Brissot P, Swinkels DW, et al. EMQN best practice guidelines for the molecular genetic diagnosis of hereditary hemochromatosis (HH). *Eur J Hum Genet.* 2016;24(4):479-495. doi:10.1038/ejhg.2015.128

**2019**

Husby S, Murray JA, Katzka DA. AGA Clinical Practice Update on Diagnosis and Monitoring of Celiac Disease-Changing Utility of Serology and Histologic Measures: Expert Review. *Gastroenterology.* 2019 Mar;156(4):885-889. doi: 10.1053/j.gastro.2018.12.010. Epub 2018 Dec 19. PMID: 30578783; PMCID: PMC6409202.

**2023**

Kammermeier J, Lamb CA, Jones KDJ, et al. Genomic diagnosis and care coordination for monogenic inflammatory bowel disease in children and adults: consensus guideline on behalf of the British Society of Gastroenterology and British Society of Paediatric Gastroenterology, Hepatology and Nutrition. *Lancet Gastroenterol Hepatol.* 2023;8(3):271-286. doi:10.1016/S2468-1253(22)00337-5

**2020**

Gardner, Timothy B. MD, MS, FACP1; Adler, Douglas G. MD, FACP2; Forsmark, Chris E. MD, FACP3; Sauer, Bryan G. MD, MSc (Clin Res), FACP (GRADE Methodologist)4; Taylor, Jason R. MD5; Whitcomb, David C. MD, PhD, FACP6. ACG Clinical Guideline: Chronic Pancreatitis. *The American Journal of Gastroenterology* 115(3):p 322-339, March 2020.

**2024**

Shelton C, LaRusch J, Whitcomb DC. Pancreatitis Overview. 2014 Mar 13 [Updated 2020 Jul 2]. In: Adam MP, Mirzaa GM, Pagon RA, et al., editors. *GeneReviews* [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK190101/>



2022;13(1):91. Published 2022 Dec 28. doi:10.3390/diagnostics13010091

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## 2022

Cusi K, Isaacs S, Barb D, et al. American Association of Clinical Endocrinology Clinical Practice Guideline for the Diagnosis and Management of Nonalcoholic Fatty Liver Disease in Primary Care and Endocrinology Clinical Settings: Co-Sponsored by the American Association for the Study of Liver Diseases (AASLD). Endocr Pract. 2022;28(5):528-562. doi:10.1016/j.eprac.2022.03.010

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## 2023

Wattacheril JJ, Abdelmalek MF, Lim JK, Sanyal AJ. AGA Clinical Practice Update on the Role of Noninvasive Biomarkers in the Evaluation and Management of Nonalcoholic Fatty Liver Disease: Expert Review. Gastroenterology. 2023;165(4):1080-1088. doi:10.1053/j.gastro.2023.06.013

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## 2023

Rinella, Mary E.1; Neuschwander-Tetri, Brent A.2; Siddiqui, Mohammad Shadab3; Abdelmalek, Manal F.4; Caldwell, Stephen5; Barb, Diana6; Kleiner, David E.7; Loomba, Rohit8. AASLD Practice Guidance on the clinical assessment and management of nonalcoholic fatty liver disease. Hepatology 77(5):p 1797-1835, May 2023. | DOI: 10.1097/HEP.0000000000000323

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## 2020

Ouahed J, Spencer E, Kotlarz D, et al. Very Early Onset Inflammatory Bowel Disease: A Clinical Approach With a Focus on the Role of Genetics and Underlying Immune Deficiencies. Inflamm Bowel Dis. 2020 May 12;26(6):820-842. doi: 10.1093/ibd/izz259. PMID: 31833544; PMCID: PMC7216773.

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## REVISIONS



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**12-04-2023**

Updated policy for 01/01/2024

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**09-27-2023**

Removed "medically necessary" and added "scientifically validated" and "investigational when the above criteria is not met and for all other indications."

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**06-01-2023**

Criteria update: Hereditary Pancreatitis Multigene Panel

Formatting changes and updated references

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**01-01-2023**

Updated table, test names, and codes in policy. References updated.

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**07-01-2022**

Updated Hereditary Inflammatory Bowel Disease section and Practice Guidelines and References

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