Medical Policy

PARAMOUNT

HMO AND PPO
ELITE (MEDICARE ADVANTAGE)
MARKETPLACE

Noninvasive Tests for Hepatic Fibrosis

Policy Number: PG0252
Last Reviewed Date: 04/01/2025
Last Revised: 04/01/2025

GUIDELINES:

- **This policy does not certify benefits or authorization of benefits, which is designated by each individual policyholder terms, conditions, exclusions, and limitations contract. It does not constitute a contract or guarantee regarding coverage or reimbursement/payment. Self-Insured group specific policy will supersede this general policy when group supplementary plan document or individual plan decision directs otherwise.**
- **Paramount applies coding edits to all medical claims through coding logic software to evaluate the accuracy and adherence to accepted national standards.**
- **This medical policy is solely for guiding medical necessity and explaining correct procedure reporting used to assist in making coverage decisions and administering benefits.**

SCOPE:
X Professional
X Facility

DESCRIPTION:
Chronic liver disease is the progressive destruction of the essential and distinctive tissue of the liver. Causes of liver disease include, but may not be limited to, alcohol use, nonalcoholic fatty liver disease or either of the viruses that cause hepatitis (hepatitis B virus [HBV] or hepatitis C virus [HCV]). If the disease is left untreated, it can result in hepatic fibrosis, cirrhosis, and eventually liver failure.

Hepatic fibrosis is the excessive accumulation of fibrotic connective tissue resulting from prolonged inflammation and progressive scarring of the liver due to a sustained wound-healing response to liver injury. The increased fibrosis and liver stiffness reduces blood flow through the liver, which leads to hardening and death of liver cells.

Noninvasive imaging technologies to detect liver fibrosis or cirrhosis among patients with chronic liver disease are being evaluated as alternatives to liver biopsy. There are two options for noninvasive monitoring: (1) multianalyte serum assays with algorithmic analysis of either direct or indirect biomarkers; and (2) specialized radiologic methods.

Specialized Radiologic Methods:
Elastography is a noninvasive, ultrasound image technique utilized to evaluate tissue elasticity or stiffness by measuring tissue displacement/distortion using ultrasonography or magnetic resonance compression. Elastography procedures include:

- Vibration-controlled transient elastography (VCTE), also known as transient elastography (TE). This technique is used mainly by the FibroScan® system.
- Magnetic resonance elastography (MRE).
- Acoustic radiation force impulse imaging (ARFI).
- Shear wave elasticity (SWE).
- Real-time tissue elastography (RTE).

Transient elastography (TE) (e.g., FibroScan), also known as Vibration-controlled transient elastography (VCTE), involves a mechanical vibrator to produce mild amplitude and low frequency waves, inducing an elastic shear wave, in patients suspected of or known to have chronic liver disease, to produce a one-dimensional

image of tissue stiffness. TE is based on the principle that fibrosis changes the elasticity and viscosity of tissue. By assessing the propagation of acoustic waves through liver tissue, the extent of fibrosis can be measured. Monitoring of the tissue compression and decompression with ultrasonography enables calculation of liver stiffness. Increases in liver fibrosis also increase liver stiffness and resistance of liver blood flow. TE does not perform as well in patients with ascites, higher body mass index, or narrow intercostal margins. Although FibroScan may be used to measure fibrosis, unlike liver biopsy, it does not provide information on necroinflammatory activity and steatosis, nor is it accurate during acute hepatitis or hepatitis exacerbations.

Magnetic resonance elastography (MRE) involves a pneumatic driver activated by a special MRE pulse sequence producing a color-scaled, quantitative, three-dimensional image. The pulse sequence is sensitive to the transmission of waves through the tissue. MRE has several advantages over ultrasound elastography, including: (1) the ability to analyze larger liver volumes; (2) the ability to analyze liver volumes of obese patients or patients with ascites; and (3) the ability to precisely analyze viscoelasticity using a 3-dimensional displacement vector.

Acoustic radiation force impulse (ARFI) elastography is a noninvasive method for detecting and staging hepatic fibrosis. ARFI involves acoustic waves from a focused ultrasonographic beam creating a qualitative two-dimensional image. This creates a ‘push’ technique inside the tissue using the acoustic radiation force from a focused ultrasound beam. Softer tissue is more easily pushed than stiffer tissue, thus creating a map a tissue stiffness.

Shear wave elasticity (SWE) involves measuring the shear waves produced from focus beams of ultrasound energy from conventional transducers producing movement within the tissue. The process provides a 2-dimensional map of tissue elasticity or stiffness.

Real-time tissue elastography (RTE) evaluates reproducible differences in backscattered ultrasound signals that result from compression of tissues and uses color Doppler to generate an image of tissue movement in response to the external vibrations. RTE can be performed in patients with ascites or inflammation.

Multianalyte Serum Assays with Algorithmic Analysis of either Direct or Indirect Biomarkers:

Liver Fibrosis Serum Panels

Blood serum laboratory tests have been developed as an alternative to liver biopsy to purportedly determine the extent of liver damage that has occurred in an individual with liver disease. Examples of these panels include, but may not be limited to:

- ASH FibroSure (ASH test)
- Enhanced liver fibrosis (ELF) test
- FibroMeter
- FibroSpect II
- FibroTest (also known as FibroSure)
- HepaScore
- LiverFASt
- NIS4
- OWLiver test

ASH FibroSure (ASH test) is utilized to reportedly assess the liver fibrosis in an individual with alcoholic liver disease. The NASH FibroSure test is utilized in an individual with NAFLD. These tests include the biomarkers listed for FibroTest with the addition of total cholesterol, triglycerides, and fasting glucose in combination with age, gender, height, and weight and generate a fibrosis score utilizing proprietary algorithms.

Enhanced liver fibrosis (ELF) test reportedly assesses the risk of progression to cirrhosis in NAFLD by measuring the following 3 markers: hyaluronic acid (HA), tissue inhibitor of matrix metalloproteinase 1 (TIMP-1) and procollagen III amino-terminal peptide (PIIINP). The ELF test is also purportedly being

utilized to assess the likelihood of progression to cirrhosis and liver-related clinical events due to NASH using a generated proprietary algorithm.

FibroMeter is utilized to measure liver fibrosis in individuals with NAFLD. It measures platelet count, prothrombin index, AST, ALT, blood urea nitrogen, HA, and age. Using a proprietary algorithm, the results of the measurements are converted into a score to determine an individual's fibrosis score.

FibroSpect II measures 3 markers for liver fibrosis: serum HA, TIMP-1, and alpha2-macroglobulin (A2M). Using a proprietary algorithm, the results of the measurements are converted into a score to determine an individual's fibrosis score.

FibroTest (also known as FibroSure) measures markers for liver fibrosis. These measurements consist of a proprietary algorithm of fibrosis markers combined with an individual's age and gender to determine liver fibrosis severity. ActiTest has been added to FibroTest, which uses the scores from FibroTest with the addition of the biomarker ALT to reportedly measure necroinflammatory activity. The biomarkers for these tests include the following:

- o A2M
- o ALT (ActiTest)
- o Apolipoprotein A1
- o Gamma-glutamyl transpeptidase (GGT)
- o Haptoglobin
- o Total bilirubin

HepaScore measures 4 markers for liver fibrosis: bilirubin, GGT, HA, A2M and applies the results to a proprietary algorithm, combined with an individual's age and sex, to determine a liver fibrosis score.

LiverFASt combines 10 biomarkers along with a proprietary algorithm that reportedly measures fibrosis as well as inflammatory activity and steatosis. The biomarkers included in the test are A2M, ALT, haptoglobin, AST, apolipoprotein, fasting glucose, total bilirubin, triglyceride, GGT and total cholesterol.

NIS4 is an emerging test that is designed to reportedly identify the presence of at-risk NASH. Supposedly, an individual who is determined to be at-risk for NASH could face increased likelihood of progression to more severe complications such as cirrhosis or cancer. The test purportedly uses a multimarker-based proprietary algorithm that integrates the following biomarkers: miR-34a-5p, A2M, YKL-40 and HbA1c.

OWLiver test for fatty liver disease is a noninvasive test that combines 28 biomarkers (metabolites) from a blood sample that are analyzed together in 2 proprietary algorithms to reportedly determine or approximate an individual's liver status regarding fibrosis.

POLICY:

Paramount Commercial Insurance Plans and Elite (Medicare Advantage) Plans

The following non-invasive elastography tests for hepatic fibrosis are covered without a prior authorization when the coverage criteria below are met:

- **Vibration-controlled transient elastography (VCTE), transient elastography (TE). (e.g., FibroScan)**
- **Magnetic resonance elastography (MRE)**
- **Acoustic radiation force impulse imaging (ARFI)**

Non-invasive elastography tests for any other indication is considered experimental/investigational, including but not all-inclusive, breast, thyroid, and melanoma.

A single FibroSURE multianalyte assay may be considered medically necessary for the evaluation of individuals with chronic liver disease.

FibroSURE multianalyte assays are considered investigational for monitoring of individuals with chronic liver disease.

Other multianalyte assays with algorithmic analyses are considered investigational for the evaluation or monitoring of individuals with chronic liver disease.

COVERAGE CRITERIA:

Paramount Commercial Insurance Plans and Elite (Medicare Advantage) Plans

Paramount considers transient elastography (TE), vibration-controlled transient elastography (VCTE) (e.g., FibroScan) medically indicated:

- To detect or stage advanced hepatic (liver) fibrosis and cirrhosis;
- Member has hepatitis B, hepatitis C, chronic alcoholic liver disease and/or all other chronic liver diseases;
- Prior to the use of liver-directed hemophilia gene therapy.

Paramount considers magnetic resonance elastography (MRE) medically indicated:

- To assess individuals with non-alcoholic fatty liver disease, distinguishing hepatic cirrhosis from non-cirrhosis, with a high risk of cirrhosis.
- Risk factors include:
    - Advanced age (65 years old or greater),
    - Obesity (BMI 30 or higher),
    - Diabetes and/or alanine aminotransferase (ALT) greater than twice the upper limit of normal.

Performance of transient elastography and/or magnetic resonance elastography more than twice per year or within 6 months following a liver biopsy (or other test for liver fibrosis) is considered not medically necessary.

Transient elastography and magnetic resonance elastography are considered experimental/investigational for all other indications.

Acoustic radiation force impulse

Paramount considers acoustic radiation force impulse imaging (ARFI) medically indicated when used to conjunctions with simple biomarkers (e.g., Fib4 and/or APRI) in the evaluation Hepatitis C as an alternative to liver biopsy.

Acoustic radiation force impulse imaging (ARFI) is considered experimental and investigational and/or unproved for all other indications.

FibroSURE

A single FibroSURE multianalyte assay may be considered medically necessary for the initial evaluation of individuals with chronic liver disease.

FibroSURE multianalyte assays are considered experimental/investigational for monitoring of individuals with chronic liver disease.

Other multianalyte assays with algorithmic analyses are considered experimental / investigational for the initial evaluation or monitoring of individuals with chronic liver disease.

Exclusions:

The following procedures are considered experimental/investigational because the effectiveness of these approaches has not been established (not an all-inclusive listing):

- Transient elastography for routine follow-up of liver transplant recipients;

- Artificial intelligence in distinguishing healthy versus Nonalcoholic fatty liver disease (NAFLD)/non-alcoholic steatohepatitis (NASH), fibrosis versus non-fibrosis in the evaluation of NAFLD progression, as well as screening and early diagnosis of fatty liver disease;
- FibroTest-ActiTest/HCV-FibroSure for all other indications (e.g., diagnosis and/or monitoring of primary biliary cholangitis);
- Hepatic artery resistive index for evaluation of fibrosis progression in individuals with non-alcoholic fatty liver disease (NAFLD);
- Magnetic resonance elastography for distinguishing hepatic cirrhosis from non-cirrhosis in persons with hepatitis C or other chronic liver diseases, and for all other indications (e.g., diagnosis of hepatic fibrosis, prediction of ascites in persons with chronic liver disease);
- Quantitative magnetic resonance (e.g., LiverMultiScan) for analysis of liver tissue composition;
- Serum ferritin as a biomarker for detecting or monitoring hepatic fibrosis in persons with hepatitis C or other chronic liver diseases (e.g., NAFLD);
- Transient elastography for detection of esophageal varices in individuals with cirrhosis, diagnosis of acute cellular rejection following liver transplantation, diagnosis of glycogenic hepatopathy, diagnosis of portal hypertension, and evaluation of alpha-1 antitrypsin deficiency, Alagille syndrome, and Gilbert syndrome;
- The following serum marker tests for detecting or monitoring hepatic fibrosis in persons with hepatitis C or other chronic liver diseases (e.g., NAFLD) because their effectiveness for these indications has not been established (not an all-inclusive list):
  - Angiotensin converting enzyme
  - Real-time tissue elastography (RTE) (e.g., HI VISION Preirus) **(0346T)**
  - FibroMAX
  - FibroSpect (FIBROSpect or FIBROSpect II)
  - HepaScore
  - LIVERFAST
  - Micro-fibrillar associated glycoprotein 4 (MFAP4)
  - MicroRNA-21
  - miR-29a and miR-122
  - miRNA-221 and miRNA-222
  - Aspartate aminotransferase (AST) to platelet ratio (APRI)
  - FIB-4
  - HCV FibroSURE or FibroTest (More than a single FibroSURE multianalyte assay is considered not medically necessary and, therefore, not covered because the available published peer-reviewed literature does not support its use for the evaluation of individuals with chronic liver disease, since each FibroSURE multianalyte assay is exclusive to a specific etiology for chronic liver disease (i.e., hepatitis C virus, alcoholic liver disease (ALD), nonalcoholic fatty liver disease (NAFLD)).
  - ASH FibroSURE **(0002M)**
  - NASH FibroSURE **(0003M)**
  - Plasma cytokeratin-18
  - Signal-induced proliferation-associated 1 like 1 (SIPA1L1).

CODING/BILLING INFORMATION

The inclusion or exclusion of a code in this section does not necessarily indicate coverage. Codes referenced in this clinical policy are for informational purposes only.
Codes that are covered may have selection criteria that must be met.
Payment for supplies may be included in payment for other services rendered.

CPT CODES	
76391	Magnetic resonance (e.g., vibration) elastography
76981	Ultrasound, elastography; parenchyma (e.g., organ)
76982	Ultrasound, elastography; first target lesion
76983	Ultrasound, elastography; each additional target lesion (List separately in addition to code for

	primary procedure)
81517	Liver disease, analysis of 3 biomarkers (hyaluronic acid [HA], procollagen III amino terminal peptide [PIIINP], tissue inhibitor of metalloproteinase 1 [TIMP-1]), using immunoassays, utilizing serum, prognostic algorithm reported as a risk score and risk of liver fibrosis and liver-related clinical events within 5 years
81596	Infectious disease, chronic hepatitis C virus (HCV) infection, six biochemical assays (ALT, A2-macroglobulin, apolipoprotein A-1, total bilirubin, GGT, and haptoglobin) utilizing serum, prognostic algorithm reported as scores for fibrosis and necroinflammatory activity in liver
81599	Unlisted multianalyte assay with algorithmic analysis
82172	Apolipoprotein, each
82247	Bilirubin; total
82977	Glutamyltransferase, gamma (GGT)
83010	Haptoglobin; quantitative
83520	Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; quantitative, not otherwise specified
83883	Nephelometry, each analyte not elsewhere specified
91200	Liver elastography, mechanically induced shear wave (eg, vibration), without imaging, with interpretation and report
0002M	Liver disease, ten biochemical assays (ALT, A2-macroglobulin, apolipoprotein A-1, total bilirubin, GGT, haptoglobin, AST, glucose, total cholesterol and triglycerides) utilizing serum, prognostic algorithm reported as quantitative scores for fibrosis, steatosis and alcoholic steatohepatitis (ASH)
0003M	Liver disease, ten biochemical assays (ALT, A2-macroglobulin, apolipoprotein A-1, total bilirubin, GGT, haptoglobin, AST, glucose, total cholesterol and triglycerides) utilizing serum, prognostic algorithm reported as quantitative scores for fibrosis, steatosis and nonalcoholic steatohepatitis (NASH)
0648T	Quantitative magnetic resonance for analysis of tissue composition (eg, fat, iron, water content), including multiparametric data acquisition, data preparation and transmission, interpretation and report, obtained without diagnostic MRI examination of the same anatomy (eg, organ, gland, tissue, target structure) during the same session; single organ **Not Covered**
0649T	Quantitative magnetic resonance for analysis of tissue composition (eg, fat, iron, water content), including multiparametric data acquisition, data preparation and transmission, interpretation and report, obtained with diagnostic MRI examination of the same anatomy (eg, organ, gland, tissue, target structure) during the same session; single organ **Not Covered**
0166U	Liver disease, 10 biochemical assays (α2-macroglobulin, haptoglobin, apolipoprotein A1, bilirubin, GGT, ALT, AST, triglycerides, cholesterol, fasting glucose) and biometric and demographic data, utilizing serum, algorithm reported as scores for fibrosis, necroinflammatory activity, and steatosis with a summary interpretation **Not Covered**
0344U	Hepatology (nonalcoholic fatty liver disease [NAFLD]), semiquantitative evaluation of 28 lipid markers by liquid chromatography with tandem mass spectrometry (LC-MS/MS), serum, reported as at-risk for nonalcoholic steatohepatitis (NASH) or not NASH **Not Covered**
0468U	Hepatology (nonalcoholic steatohepatitis [NASH]), miR-34a-5p, alpha 2-macroglobulin, YKL40, HbA1c, serum and whole blood, algorithm reported as a single score for NASH activity and fibrosis **Not Covered**

REVISION HISTORY EXPLANATION: ORIGINAL EFFECTIVE DATE: 10/24/2014

Date	Explanation & Changes
10/24/2014	• Policy created to reflect most current clinical evidence per TAWG
12/02/2014	• Added new 2015 CPT code 91200
07/09/2015	• Changed title from Elastography to Ultrasound Transient Elastography. Transient elastography is now covered
08/20/2015	• Transient elastography (91200) will no longer require prior authorization • Procedure 0346T is non-covered

	• Policy reviewed and updated to reflect most current clinical evidence per TAWG
03/13/2018	• Changed title from Ultrasound Transient Elastography to Noninvasive Tests for Hepatic Fibrosis. • Added codes 0001M-0003M as non-covered for all product lines • Added these non-invasive tests for hepatic fibrosis as non-covered for all product lines: Acoustic radiation force impulse imaging (ARFI) (e.g., Virtual Touch Imaging – Acuson S2000-3000), Magnetic resonance elastography (MRE), FibroMAX, FibroSpect, HepaScore, Aspartate aminotransferase (AST) to platelet ratio (APRI), FIB-4, HCV FibroSURE or FibroTest (0001M), ASH FibroSURE (0002M), & NASH FibroSURE (0003M) • Policy reviewed and updated to reflect most current clinical evidence per Medical Policy Steering Committee
09/24/2019	• Changed title from Noninvasive Tests for Hepatic Fibrosis to Elastography • Updated with the 2019 CPT codes • Added allowed/covered diagnosis codes • Determined coverage for Transient elastography (TE), Magnetic resonance elastography (MRE), Acoustic radiation force impulse imaging (ARFI) related to cirrhosis of liver
12/18/2020	• Medical policy placed on the new Paramount Medical Policy Format
02/16/2023	• Medical Policy updated to reflect Medicaid coverage to Anthem as of 02/01/2023
04/01/2024	• Medical Policy reviewed and updated to reflect the most current clinical evidence • Changed policy title from Elastography to Noninvasive Tests for Hepatic Fibrosis • Added documentation related to Multianalyte Serum Assays with Algorithmic Analysis of either Direct or Indirect Biomarkers • Added “A single FibroSURE multianalyte assay may be considered medically necessary for the initial evaluation of patients with chronic liver disease.” • Added “FibroSURE multianalyte assays are considered experimental/investigational for monitoring of individuals with chronic liver disease.” • Added “Other multianalyte assays with algorithmic analyses are considered experimental / investigational for the initial evaluation or monitoring of individuals with chronic liver disease.” • Removed deleted procedure code 0001M • Added noncovered procedure codes 0648T, 0649T, 0116U, 0344U • Added covered procedure codes 0002M, 0003M, 81517
04/01/2025	• Medical Policy reviewed and updated to reflect the most current clinical evidence • Added non-covered code 0468U, effective 07/01/2024

Paramount reserves the right to review and revise our policies periodically when necessary. When there is an update, we will publish the most current policy to https://www.paramounthealthcare.com/providers/medical-policies/policy-library

REFERENCES/RESOURCES

Centers for Medicare and Medicaid Services, CMS Manual System and other CMS publications and services https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Internet-Only-Manuals-IOMs

American Medical Association, *Current Procedural Terminology (CPT®)* and associated publications and services https://www.ama-assn.org/amaone/cpt-current-procedural-terminology

Centers for Medicare and Medicaid Services, Healthcare Common Procedure Coding System, HCPCS Release and Code Sets https://www.cms.gov/Medicare/Coding/HCPCSReleaseCodeSets/HCPCS-Quarterly-

Update

U.S. Preventive Services Task Force, https://www.uspreventiveservicestaskforce.org/uspstf/ Industry Standard Review

Hayes, Inc., https://www.hayesinc.com/

Industry Standard Review