of Tennessee

Policy

Reimbursement Policy

Serum Testing for Hepatic Fibrosis in the Evaluation and Monitoring of Chronic Liver Disease

I. Policy Description

Chronic liver disease (CLD) refers to a wide range of liver pathologies that include inflammation (chronic hepatitis), liver cirrhosis, and hepatocellular carcinoma.

Hepatic fibrosis is associated with a cycle of extracellular matrix deposition and degradation. Biomarkers of extracellular matrix turnover are used to directly assess fibrosis and, theoretically, to monitor progression or regression.[1] These markers include several glycoproteins, members of the collagen family, collagenases and their inhibitors, and several cytokines involved in the fibrogenic process.[1] The markers may be utilized individually, as well as in panel combinations.[2]

II. Indications and/or Limitations of Coverage

Application of coverage criteria is dependent upon an individual's benefit coverage at the time of the request. Specifications pertaining to Medicare and Medicaid can be found in the "Applicable State and Federal Regulations" section of this policy document.

1) For individuals with a chronic hepatitis B (HBV) or chronic hepatitis C (HCV) viral infection, FibroSURE® (i.e., HBV FibroSURE®, HCV FibroSURE®), ELF™(ELFTM), **or** FibroTest® testing once every six months **MEETS COVERAGE CRITERIA.**

2) For individuals with metabolic dysfunction-associated steatotic liver disease (MASLD) (including metabolic dysfunction-associated steatohepatitis [MASH]), **or** alcoholic hepatitis, or to rule out compensated advanced chronic liver disease (cACLD) for individuals with an elevated liver stiffness measurement, ELF™(ELFTM) **or** FibroTest® testing once every six months **MEETS COVERAGE CRITERIA.**

3) For all situations, including for individuals with any of the conditions described above, the use of other multianalyte assays with algorithmic analysis (e.g., ASH FibroSURE®, LIVERFASt™, NASH FibroSURE®, OWLiver®) **DOES NOT MEET COVERAGE CRITERIA**.

4) For individuals with liver disease not meeting the above criteria, the use of ELF™(ELFTM), FibroTest®, HBV FibroSURE®, **and/or** HCV FibroSURE® **DOES NOT MEET COVERAGE CRITERIA**.

The following does not meet coverage criteria due to a lack of available published scientific literature confirming that the test(s) is/are required and beneficial for the diagnosis and treatment of an individual's illness.

5) Except when included as a component of one of the multianalyte assays described above, the use of the following serum biomarkers in the diagnosis, prognosis, or monitoring of chronic liver disease **DOES NOT MEET COVERAGE CRITERIA**:
   a) Signal-induced proliferation-associated 1 like 1 (SIPA1L1)
   b) microRNA (miRNA or miR) analysis, including but not limited to, the following:
      i) microRNA-21 (miRNA-21 or miR-21)
      ii) miRNA-29a (miR-29a)
      iii) miRNA-122 (miR-122)
      iv) miRNA-221 (miR-221)
      v) miRNA-222 (miR-222)
   c) Chitinase 3-like 1 (CHI3L1)
   d) Hyaluronic acid
   e) Type III procollagen (PCIII)
   f) Type IV collagen
   g) Laminin
   h) Plasma caspase-generated cytokeratin-18
   i) Micro-fibrillar associated glycoprotein 4 (MFAP4)

III. Applicable State and Federal Regulations

DISCLAIMER: If there is a conflict between this Policy and any relevant, applicable government policy for a particular member [e.g., Local Coverage Determinations (LCDs) or National Coverage Determinations (NCDs) for Medicare and/or state coverage for Medicaid], then the government policy will be used to make the determination. For the most up-to-date Medicare policies and coverage, please visit the Medicare search website: https://www.cms.gov/medicare-coverage-database/search.aspx. For the most up-to-date Medicaid policies and coverage, visit the applicable state Medicaid website.

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Food and Drug Administration (FDA)

Many labs have developed specific tests that they must validate and perform in house. These laboratory-developed tests (LDTs) are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88). LDTs are not approved or cleared by the U. S. Food and Drug Administration; however, FDA clearance or approval is not currently required for clinical use.

IV. Applicable CPT/HCPCS Procedure Codes

CPT	Code Description
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 Proprietary test: HCV FibroSURE™, FibroTest™ Laboratory/Manufacturer: BioPredictive S.A.S
81599	Unlisted multianalyte assay with algorithmic analysis
84999	Unlisted chemistry procedure
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) Proprietary test: ASH FibroSURE™ Laboratory/Manufacturer: BioPredictive S.A.S
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) Proprietary test: NASH FibroSURE™ Laboratory/Manufacturer: BioPredictive S.A.S
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

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CPT	Code Description
	Proprietary test: LiverFASt™ Lab/Manufacturer: Fibronostics
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 Proprietary test: OWLiver® Lab/Manufacturer: CIMA Sciences, LLC
0468U	Hepatology (nonalcoholic steatohepatitis [NASH]), miR-34a5p, alpha 2-macroglobulin, YKL40, HbA1c, serum and whole blood, algorithm reported as a single score for NASH activity and fibrosis Proprietary test: NASHnextTM (NIS4TM) Lab/Manufacturer: Labcorp

Procedure codes appearing in Medical Policy documents are included only as a general reference tool for each policy. They may not be all-inclusive.

V. Evidence-based Scientific References

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VI. Revision History

Revision Date	Summary of Changes
09/04/2025	Reviewed and Updated: Updated background, guidelines, and evidence-based scientific references. Literature review necessitated the following changes in coverage criteria: HBV and HCV allowed tests (all 4) broken out from MASLD, MASH, and AH, revised CC1 now reads: "1) For individuals with a chronic hepatitis B (HBV) or chronic hepatitis C (HCV) viral infection, FibroSURE® (i.e., HBV FibroSURE®, HCV FibroSURE®), ELF™(ELFTM), or FibroTest® testing once every six months MEETS COVERAGE CRITERIA." Only ELF and FibroTest are appropriate for MASLD, MASH, and AH, these conditions are now found in CC2. Added elevated LSM to rule out cACLD as an appropriate reason for ELF and FibroTest. New CC2 now reads: "2) For individuals with metabolic dysfunction-associated steatotic liver disease (MASLD) (including metabolic dysfunction-associated steatohepatitis [MASH]), or alcoholic hepatitis, or to rule out compensated advanced chronic liver disease (cACLD) for individuals with an elevated liver stiffness measurement, ELF™(ELFTM) or FibroTest® testing once every six months MEETS COVERAGE CRITERIA." Former CC2, CC3, and CC4, now CC3, CC4, and CC5, edited for clarity, now read: "3) For all situations, including for individuals with any of the conditions described above, the use of other multianalyte assays with algorithmic analysis

	(e.g., ASH FibroSURE®, LIVERFAStTM, NASH FibroSURE®, OWLiver®) DOES NOT MEET COVERAGE CRITERIA. 4) For individuals with liver disease not meeting the above criteria, the use of ELF™(ELFTM), FibroTest®, HBV FibroSURE®, and/or HCV FibroSURE® DOES NOT MEET COVERAGE CRITERIA. 5) Except when included as a component of one of the multianalyte assays described above, the use of the following serum biomarkers in the diagnosis, prognosis, or monitoring of chronic liver disease DOES NOT MEET COVERAGE CRITERIA:" Removed CPT code 88341, 88342