Policy Number: PA.101.MPC
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PA.101.MPC Noninvasive Tests for Hepatic Fibrosis

This policy covers the following noninvasive tests for hepatic fibrosis:

- **Enhanced Liver Fibrosis (ELF) test**
- **Fibro Test-Acti Test/HCV-Fibrosure**
- **Magnetic Resonance Elastography**
- **Transient Elastography (TE) (e.g., Fibroscan)**

Maryland Physicians Care considers the following non-invasive blood tests medically necessary for the detection and prognosis of liver fibrosis in persons with chronic liver diseases.

Enhanced Liver Fibrosis (ELF™) test: measures three direct markers of fibrosis: hyaluronic acid (HA), procollagen III amino-terminal peptide (PIIINP), and tissue inhibitor of matrix metalloproteinase 1 (TIMP-1),

Fibro Test (FT) - Acti Test/HCV- Fibrosure: consists of an algorithm of five fibrosis markers (alfa2-macroglobulin, apolipoproteinA1, haptoglobin, GGT, bilirubin, plus alanine aminotransferase)

Criteria

- Evaluating hepatic fibrosis in chronic hepatitis C patients
- Diagnosing fibrosis in carriers of chronic hepatitis B virus
- Evaluating hepatic fibrosis in co-infected HIV carriers
- Providing access to new-generation non-interferon treatment for hepatitis
- Evaluating fibrosis in patients suffering from metabolic conditions (nonalcoholic
- fatty liver disease) and patients who consume excess alcohol

Limitations:
Defer the test in transient situations that could modify the components of FibroTest-ActiTest, such as:

- Acute hemolysis, which could decrease haptoglobin and increase unconjugated bilirubin

- Acute hepatitis, whether drug-induced, viral (superinfection by hepatitis A virus: HAV, hepatitis B virus: HBV, Epstein-Barr virus: EBV), or autoimmune. Massive hepatic necrosis leads to a large increase of transaminases and total bilirubin.

- Acute inflammation, as with concomitant bacterial or acute viral infection: bronchopulmonary or urinary tract infection. The large increase of haptoglobin can lead to false-negative results.

- Extrahepatic cholestasis, such as gallstones

The advice of a liver disease specialist should be sought for interpretation in chronic states in which the components of the test could be modified, such as chronic hemolysis, particularly in patients with a cardiac valvular prosthesis; Gilbert disease; protease inhibitors used in HIV treatment, which can increase unconjugated bilirubin (Indinavir, Atazanavir); or gamma glutamyltransferase (GGT) and alanine aminotransferase (Ritonavir).

- Performance of this test more than twice per year is considered not medically necessary.
- Performance of this test within 6 months following a liver biopsy or transient elastography is considered not medically necessary.
- This test is considered experimental and investigational for all other indications.

Background:
Fibrosis and inflammatory activity are the 2 main causes of liver disease.

FibroTest-ActiTest estimates the levels of fibrosis and cirrhosis in the liver as well as the level of necroinflammatory activity. The estimation is made by measuring 5 fibrosis markers (gamma-glutamyl transferase, total bilirubin, alpha-2-macroglobulin, apolipoprotein A1, haptoglobin, plus alanine aminotransferase). The activity score is a measure of liver inflammation caused by disease. Results from these tests are combined with the patient's age and sex to estimate hepatic fibrosis and inflammatory activity scores.

Hepatic fibrosis is typically compared to a form of scar tissue that progresses throughout the liver. The most serious stage of fibrosis is known as cirrhosis.

Magnetic Resonance Elastography: Maryland Physicians Care considers magnetic resonance elastography medically necessary for
non-alcoholic steatohepatitis (NASH), and hepatic fibrosis or cirrhosis is known or syspected

Maryland Physicians Care considers **magnetic resonance elastography** experimental and investigational for distinguishing hepatic cirrhosis from non-cirrhosis in persons with hepatitis C or other chronic liver diseases, and for all other indications (e.g., prediction of ascites in persons with chronic liver disease) because its effectiveness for these indications has not been established.

PA.101.MPC Transient Elastography (e.g., FibroScan)

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Transient Elastography (TE) (e.g., FibroScan): Maryland Physicians Care considers transient elastrography medically necessary for the following indications:

- Initial assessment of fibrosis of members with a diagnosis with hepatitis C; or
- Follow-up assessment of fibrosis of members with a diagnosis of hepatitis C and previously documented F0, F1, or F2 per METAVIR staging guidelines; or
- Assessment of advanced fibrosis (F2 or greater) versus minimal or no fibrosis (F1 or F0)

NOTE: TE is considered experimental and investigational for all other indications.

Limitations

TE (e.g. FibroScan) is considered not medically necessary and is therefore not covered if the member meets any of the following criteria:

- BMI of <19 kg/m2 or >30 kg/m2
- Ascites
- Focal lesions within the liver (e.g., tumor)
- Acute liver injury
- Previously documented liver fibrosis of F3 or F4
- Pregnant
- Alanine transaminase (ALT) level five or more times the upper limit of normal (55 units per liter)
- Implanted metal device (e.g., pacemaker, automated implantable cardioverter defibrillator (AICD), or any other implantable defibrillators)
- TE performed within the previous 12 months
- Liver biopsy within the previous six months

Experimental and Investigational: The following are considered experimental and investigational for the detection or monitoring of 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)

- Acoustic Radiation Forced Impulse (ARFI)
- Hepatic Artery Resistive Index
- Serum Marker Tests including:
  - Angiotensin converting enzyme
  - b. FibroMAX
  - c. FibroSpect
  - d. HepaScore
  - e. LIVERFAST
  - f. Micro-fibrillar associated glycoprotein 4 (MFAP4)

- g. MicroRNA-21
- h. miR-29a and miR-122
- i. miRNA-221 and miRNA-222
- j. NASH FibroSure
- k. Plasma cytokeratin-18
- l. Signal-induced proliferation associated 1 like 1 (SIPA1L1)

Background

Fibrosis is a scarring process that replaces damaged liver cells, causing inflammation and leading to the formation of fibrous scar tissue in the liver. Transient Elastography (TE) is a non-invasive technique for the evaluation of fibrosis in chronic liver disease. TE serves as an alternative to liver biopsy, the gold standard for evaluating liver fibrosis. TE measures liver stiffness by tracking the wave speed through ultrasound.

The only system suitable for performing TE is the FibroScan System (Echosens SA; Paris, France), as approved by the US FDA on April 5, 2013.

METAVIR Scoring System

Activity Grade	
A0	No activity
A1	Mild activity
A2	Moderate activity
A3	Severe activity
Fibrosis Stage	
F0	No fibrosis
F1	Fibrosis portal expansion (mild fibrosis)
F2	Few bridges or septa (moderate fibrosis)
F3	Numerous bridges or septa (severe fibrosis)
F4	Cirrhosis

Codes:

0014M	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 (ELF™)
76391	Magnetic resonance (eg, vibration) elastography

76981	Ultrasound, elastography; parenchyma (eg, organ)
76982	Ultrasound, elastography; first target lesion
76983	Ultrasound, elastography; each additional target lesion (List separately in addition to code for primary procedure)
81596	FibroTest-ActiTest, Serum 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
91200	Liver elastography, mechanically induced shear wave (e.g., vibration), without imaging, with interpretation and report

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