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PA.101.MPC Noninvasive Tests for Hepatic Fibrosis

This policy covers the following noninvasive tests for the detection and prognosis of liver fibrosis in persons with chronic liver diseases [1, 2, 3]:

- **Enhanced Liver Fibrosis (ELF) serologic test:** measures three direct markers of fibrosis: hyaluronic acid (HA), N-terminal propeptide of procallagen type III (PIIINP), and tissue inhibitor of metalloproteinase 1 (TIMP-1)
- **Fibro Test (aka., FibroSure) and ActiTest (FT-AT) serologic tests:** consists of five standard biochemical markers (alfa-2-macroglobulin (A2M), apolipoprotein A1, haptoglobin, gamma-glutamyltransferase (GGT), and total bilirubin)
- **Magnetic Resonance Elastography (MRE)**
- **Transient Elastography (TE) (e.g., Fibroscan)**

Criteria [4]

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

Imaging

- Magnetic resonance elastography (MRE) [4,5]:
  - Metabolic dysfunction-associated steatohepatitis (MASH)
  - Known or suspected hepatic fibrosis or cirrhosis
- Transient elastography (TE) [5]:
  - Initial assessment of fibrosis in diagnosed hepatitis C
  - Follow-up assessment of fibrosis in diagnosed hepatitis C and previously documented F0, F1, or F2 per METAVIR staging guidelines

Assessment of advanced fibrosis (≥ F2) versus no or minimal fibrosis (F0 – F1)

Limitations

Clinical factors that could affect the assessment of hepatic fibrosis in the following noninvasive tests include:

- **ELF [4]**

  - Gastrectomy – increases HA
  - Extra-hepatic fibrosing conditions – conditions such as interstitial lung disease can increase collagen markers
- **FibroTest** [4]
  - Active alcohol use – increases GGT
  - Inflammatory condition – increased A2M levels and falsely elevated FibroTest
  - Hemolysis – decreases haptoglobin levels and increases total bilirubin
  - Gilbert syndrome and other cholestatic diseases – increased total bilirubin
  - Acute sickle cell crisis – related to hemolysis
- **MRE** [4]
  - Ascites – large amounts can lead to test failure
  - Iron overload – affects T2 signaling leading to test failure
- **TE** [4]
  - Narrow interstitial space
  - Ascites – affects transmission of vibration and mechanical signals
  - Moderate to severe steatosis – causes overestimate fibrosis
  - Chronic kidney disease – hemofiltration can result in lower stiffness in those with baseline fluid overload
  - Acute sickle cell crisis – acute vaso-occlusive crisis increases liver stiffness

The advice of a liver disease specialist should be sought for interpretation in chronic states in which the components of the FibroTest could be modified

- 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.

Contraindications

Magnetic Resonance Elastography (MRE):

MRE is 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 not listed above in criteria (e.g., prediction of ascites in persons with chronic liver disease) because its effectiveness for these indications has not been established.

Transient Elastography (TE):

TE is considered not medically necessary and not covered if the member meets any of the following criteria:

- BMI of <19 kg/m2 or >30 kg/m2
- 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

NOTE: TE is considered experimental and investigational for all other indications not listed in the above criteria.

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
  - FibroMAX
  - FibroSpect
  - HepaScore
  - LIVERFAST
  - Micro-fibrillar associated glycoprotein 4 (MFAP4)
  - MicroRNA-21
  - miR-29a and miR-122
  - miRNA-221 and miRNA-222
  - NASH FibroSure
  - Plasma cytokeratin-18
  - Signal-induced proliferation associated 1 like 1 (SIPA1L1)

Background

METAVIR Scoring System [6]

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

CPT Codes	
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)
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	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 necro inflammatory activity in liver
91200	Liver elastography, mechanically induced shear wave (e.g., vibration), without imaging, with interpretation and report

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