

## 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.

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

Policy Number: PA.101.MPC

Last Review Date: 11/16/2023

Effective Date: 12/01/2023

- 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 glutamyl transferase (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 necro inflammatory 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 suspected.

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

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

Policy Number: PA.101.MPC

Last Review Date: 11/16/2023

Effective Date: 12/01/2023

of ascites in persons with chronic liver disease) because its effectiveness for these indications has not been established.

**Transient Elastography (TE) (e.g., FibroScan):** Maryland Physicians Care considers transient elastography 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/m<sup>2</sup> or >30 kg/m<sup>2</sup>
- 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
  - FibroMAX
  - FibroSpect
  - HepaScore

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

Policy Number: PA.101.MPC

Last Review Date: 11/16/2023

Effective Date: 12/01/2023

- 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

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

CPT 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,

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

Policy Number: PA.101.MPC

Last Review Date: 11/16/2023

Effective Date: 12/01/2023

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

### References

1. BioPredictive: Technical Recommendations for FibroTest and FibroMax assays, Bio Predictive.  
[Biopredictive.com/products/fibromax/](https://biopredictive.com/products/fibromax/)
2. Halfon P, Bourliere M, Deydier R, et al: Independent prospective multicenter validation of biochemical markers (FibroTest-ActiTest) for the prediction of liver fibrosis and activity in patients with chronic hepatitis C: the fibropaca study. *Am J Gastroenterol*. 2006 Mar;101(3):547-555. doi: 10.1111/j.1572-0241.2006.00411.x.  
<https://pubmed.ncbi.nlm.nih.gov/16542291/>
3. Houot M, Ngo Y, Munteanu M, Marque S, Poynard T: Systematic review with meta-analysis: direct comparisons of biomarkers for the diagnosis of fibrosis in chronic hepatitis C and B. *Aliment Pharmacol Thera*. 2016 Jan;43:16-29. doi: 10.1111/apt.13446.  
<https://pubmed.ncbi.nlm.nih.gov/26516104/>
4. Anastasiou J, Alisa A, Virtue S, Portmann B, Murray-Lyon I, Williams R: Noninvasive markers of fibrosis and inflammation in clinical practice: prospective comparison with liver biopsy. *Eur J Gastroenterol Hepatol*. 2010 Apr;22(4):474-480. doi: 10.1097/MEG.0b013e328332dd0a.  
<https://pubmed.ncbi.nlm.nih.gov/19887952/>
5. Martínez SM, Crespo G, Navasa M, Forns X: Noninvasive assessment of liver fibrosis. *Hepatology*. 2011 Jan;53(1):325-335. doi: 10.1002/hep.24013.  
<https://pubmed.ncbi.nlm.nih.gov/21254180/>
6. Afdahl NH. Fibroscan (transient elastography) for the measurement of liver fibrosis. *Gastroenterol Hepatol (NY)*. 2012 Sep;8(9):605-607.  
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3594956/>

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

Policy Number: PA.101.MPC

Last Review Date: 11/16/2023

Effective Date: 12/01/2023

7. Castera L, Foucher L, Bernard PH, et al. Pitfalls of liver stiffness measurement: a 5-year prospective study of 13,369 examinations. *Hepatology*. 2010 Mar;51(3):828-835. doi: 10.1002/hep.23425.  
<http://onlinelibrary.wiley.com/doi/10.1002/hep.23425/full>
8. Crespo G, Fernandez-Varo G, Marino Z, et al. ARFI, FibroScan, ELF, and their combinations in the assessment of liver fibrosis: a prospective study. *J Hepatol*. 2012 Aug;57(2):281-287. doi: 10.1016/j.jhep.2012.03.016. Epub 2012 Apr 17.  
<http://www.sciencedirect.com/science/article/pii/S0168827812002711>
9. Degos F, Perez P, Roche B, et al. Diagnostic accuracy of FibroScan and comparison to liver fibrosis biomarkers in chronic viral hepatitis: a multicenter prospective study (the FIBROSTIC study). *J Hepatol*. 2010 Dec;53(6):1013-1021. doi: 10.1016/j.jhep.2010.05.035. Epub 2010 Aug 14.  
<http://www.sciencedirect.com/science/article/pii/S0168827810006926>
10. Foucher J, Diagnosis of cirrhosis by transient elastography (FibroScan): a prospective study. *Gut*. 2006 Mar;55(3):403-408. Epub 2005 Jul 14.  
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1856085/>
11. Friedrich-Rust M, Ong MF, Martens S, et al. Performance of transient elastography for the staging of liver fibrosis: a meta-analysis. *Gastroenterology*. 2008 Apr;134(4):960-974. doi: 10.1053/j.gastro.2008.01.034. Epub 2008 Jan 18.  
<http://www.sciencedirect.com/science/article/pii/S001650850800108X>
12. Hayes Medical Technology Directory. Ultrasound Transient Elastography for Detecting Hepatic Fibrosis in Patients with Hepatitis C. Publication Date: March 27, 2019. Annual Review: March 10, 2022.
13. HepatitisCentral.com. Table 4. The METAVIR System. Algorithm for Evaluation of Histological Activity. Copyright ©1994-2019 Hepatitis Central.  
<http://www.hepatitiscentral.com/hcv/biopsy/charts/metavir.html>
14. Kemp W, Roberts S. FibroScan® and transient elastography. *Aust Fam Physician*. 2013 Jul;42(7):468-471.  
<http://www.racgp.org.au/afp/2013/july/fibroscan/>
15. U.S. Food and Drug Administration (FDA). Echosens' FibroScan® System. 510(k) Summary. K123806. Approved: Apr. 5, 2013. (Manufacturer: Echosens SA).  
[https://www.accessdata.fda.gov/cdrh\\_docs/pdf12/k123806.pdf](https://www.accessdata.fda.gov/cdrh_docs/pdf12/k123806.pdf)
16. Wong GL. Update of liver fibrosis and steatosis with transient elastography (Fibroscan). *Gastroenterol Rep (Oxf)*. 2013 Jul;1(1):19-26. doi: 10.1093/gastro/got007. Epub 2013 Mar 26.  
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3941434/>
17. Zachary D, Goodman. Grading and staging systems for inflammation and fibrosis in chronic liver diseases. *Journal of Hepatology* 47 (2007) 598–607.  
<https://pubmed.ncbi.nlm.nih.gov/17692984/>

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

Policy Number: PA.101.MPC

Last Review Date: 11/16/2023

Effective Date: 12/01/2023

18. Yasaman Vali, et. al. Enhanced liver fibrosis test for the non-invasive diagnosis of fibrosis in patients with NAFLD: A systematic review and meta-analysis. Journal of Hepatology 2020 vol. 73 j 252–262.  
<https://pubmed.ncbi.nlm.nih.gov/32275982/>

### **Disclaimer**

Maryland Physicians Care medical payment and prior authorization policies do not constitute medical advice and are not intended to govern or otherwise influence the practice of medicine. The policies constitute only the reimbursement and coverage guidelines of Maryland Physicians Care and its affiliated managed care entities. Coverage for services varies for individual members in accordance with the terms and conditions of applicable Certificates of Coverage, Summary Plan Descriptions, or contracts with governing regulatory agencies.

Maryland Physicians Care reserves the right to review and update the medical payment and prior authorization guidelines in its sole discretion. Notice of such changes, if necessary, shall be provided in accordance with the terms and conditions of provider agreements and any applicable laws or regulations.

These policies are the proprietary information of Maryland Physicians Care. Any sale, copying, or dissemination of said policies is prohibited.