CLINICAL MEDICAL POLICY

Policy Name:	Noninvasive Assessment of Liver Fibrosis in Chronic Hepatitis C
Policy Number:	MP-009-MD-PA
Approved By:	Medical Management
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Application:	All participating hospitals and providers
Page Number(s):	1 of 9

Disclaimer

Gateway Health℠ (Gateway) medical payment and prior-authorization policy is intended to serve only as a general reference resource regarding payment and coverage for the services described. This policy does not constitute medical advice and is not intended to govern or otherwise influence medical decisions.

POLICY STATEMENT:

Gateway Health Plan® provides coverage under the medical surgical benefits of the Company's Medicaid and Medicare products for medically necessary diagnostic measures for liver disease. Diagnostic measures include: liver biopsy, noninvasive markers (e.g., FibroScan) and serological markers.

This policy is designed to address medical necessity guidelines that are appropriate for the majority of individuals with a particular disease, illness or condition. Each person's unique clinical circumstances warrants individual consideration, based upon review of applicable medical records.

(Current applicable PA HealthChoices Agreement Section V. Program Requirements, B. Prior Authorization of Services, 1. General Prior Authorization Requirements.)

DEFINITIONS:

Prior Authorization Review Panel – A panel of representatives from within the PA Department of Human Services who have been assigned organizational responsibility for the review, approval and denial of all PH-MCO Prior Authorization policies and procedures.

PROCEDURES

1. The following diagnostic testing are considered medically necessary:
   A. Liver Biopsy
   B. Radiologic Testing
      i. FibroScan
      ii. Acoustic Radiation Force Impulse (ARFI)

      The following medical necessity criteria must be met for radiologic testing:
      a. The patient with suspected diagnosis of hepatitis C virus with and is a candidate for treatment; AND
      b. Testing is being performed in order to distinguish hepatic cirrhosis from non-hepatic cirrhosis in persons with hepatitis C; AND
      c. Is only performed every six months; AND
      d. Cannot be performed within six months following a liver biopsy; AND
      e. For the patient that is actively using alcohol or IV drugs, or has a history of abuse, there is documentation by the prescriber regarding the risks of alcohol or IV drug abuse and an offer of referral for substance abuse disorder treatment

   C. Multi-Analyte Serological Testing
      i. FibroSure, FibroTest-ActiTest, FIBROSpect
      ii. HepaScore
      iii. APRI

2. Contraindications
   A. Morbid obesity (BMI >30)
   B. Ascites
   C. Pregnancy-per the manufacturer
   D. Presence of pacemaker-per the manufacturer
   E. Elevated alkaline phosphatase

3. When services are not covered
   For conditions and services other than those listed above scientific evidence has not been established.

4. Post-payment Audit Statement
   The medical record must include documentation that reflects the medical necessity criteria and is subject to audit by Gateway Health Plan® at any time pursuant to the terms of your provider agreement.

5. The place of service for all diagnostic measurements listed is outpatient.

6. Governing Bodies Approval
   On April 5th 2013, the FDA provided 510(k) clearance for the FibroScan® device as a commercially available transient elastography unit citing the high degree of reliability of measurement. FibroScan® is indicated for noninvasive measurement of shear wave speed at 50 Hz in the liver. The shear wave speed may be used an aid to clinical management of patients with liver disease.
   No Local or National Medicare Determinations were located. Therefore, the coverage criteria in this medical policy will apply to Gateway Health Plan® Medicare members.

CODING REQUIREMENTS:

Procedure Codes

CPT Code	Description
47000	Biopsy of liver, needle; percutaneous
47001	Biopsy of liver, needle; when done for indicated purpose at time of other major procedure (List separately in addition to code for primary procedure)
47100	Biopsy of liver, wedge
82172	Apolipoprotein, each
82247	Bilirubin, total
82977	Glutamyltransferase, gamma GGTP)
83010	Haptoglobin, quantitative
83519	Immunoassay, analyte quantitative by radiopharmaceutical technique (i.e., RIA)
83520	Immunoassay, analyte, quantitative; not otherwise specified (If billed for FIBROspect or HCV-FIBROSURE, FibroMAX, FibroTest-ActiTest, HepaScore)
83883	Nephelometry, each analyte not elsewhere specified (If billed for FIBROspect or HCV-FIBROSURE, FibroMAX, FibroTest-Acti-Test, HepaScore)
84450	Transferase; asparate amino (AST) (SGOT)
84460	Transferase, alanine amino (ALT) (SGPT)
88342	Immunohistochemistry or immunocytochemistry, per specimen; initial single antibody stain procedure (for the evaluation of non-alcoholic fatty liver disease and other liver disease)
91200	Liver elastography, mechanically induced shear wave (e.g., vibration), without imaging, with interpretation and report
0346T	Ultrasound, elastography (List separately in addition to code for primary procedure)

Diagnosis Codes

ICD-10 Codes	Description
B18.2	Chronic viral hepatitis C
B19.20	Unspecified viral hepatitis C without coma
B19.21	Unspecified viral hepatitis C with coma
K74.0	Hepatic fibrosis
K74.60	Unspecified cirrhosis of liver
K74.69	Other cirrhosis of liver
Z20.5	Contact with and (suspected) exposure to viral hepatitis
Z22.50	Carrier of unspecified viral hepatitis
Z22.52	Carrier of viral hepatitis C

LITERATURE SUMMARY:

Chronic hepatitis C is one of the more serious types of hepatitis that is spread through exposure to infected blood. The most common form of transmission occurs from sharing needles. Other modes of transmission include contaminated medical products during transfusion or other medical procedures. In the United States, the World Health Organization has estimated that there are 3.2 million people living with chronic hepatitis C.

One of the outcomes of chronic hepatitis C is the development of hepatic fibrosis that eventually leads to cirrhosis, liver failure and hepatocellular carcinoma. It has been reported that of those people with chronic hepatitis C, approximately 15 to 25% will require liver transplant. With these statistics, it is essential that patients with chronic hepatitis C be diagnosed and monitored for liver fibrosis. In chronic hepatitis C, quantification of the degree of live fibrosis is important for prognosis and for treatment.

For some time, liver biopsy has been considered the gold standard for the evaluation of hepatic fibrosis and for initiating treatment (Castera and Bedossa, 2011). A liver biopsy has recognized limitations including sampling error and interobserver variability (Cohen and Afdhal, 2010). However, the limitations of liver biopsy have led to the development of noninvasive procedures, such as transient elastography. While the FibroScan is 100 times larger than that of a liver biopsy (Cohen and Afdhal, 2010). The FibroScan can be expanded by sampling in different intercostal spaces. The technology is based on the noninvasive measurement of liver sear wave speed. A mechanical vibrator produces low-amplitude elastic waves that travel through the skin and intercostal space into the liver. Ultrasound is used to track the shear wave and to measure speed, which is then correlated with the elasticity of the liver.

Due to limitations of liver biopsy, noninvasive diagnostic tools and procedures have been developed to measure liver fibrosis, monitor its progression and potential response to therapy. These measure include and are not limited to transient elastography, magnetic resonance elastography, and several serum biomarkers.

The United States Preventive Services Task Force (USPSTF) suggests that noninvasive tests with good diagnostic accuracy are possible alternatives to liver biopsy for the diagnosis of fibrosis or cirrhosis and was given a Grade B recommendation (Moyer, 2014).

In 2014, the VA published a clinical guideline regarding treatment considerations for chronic hepatitis C infection. The guideline authors indicate that although liver biopsy is currently considered the best method for staging fibrosis and grading inflammation, alternatives, such as non-invasive imaging and use of fibrosis markers, may be considered instead of a biopsy, with a cautious understanding of their inherent limitations.

Castera et al (2015) reported that liver biopsy is now considered an imperfect gold standard and the procedure should be part of an integrated system with noninvasive testing and serum biomarkers.

Transient elastography (TE, FibroScan) is a novel non-invasive method that has been proposed for the assessment of hepatic fibrosis in patients with chronic liver diseases, by measuring liver stiffness. TE is a rapid and user-friendly technique that can be easily performed at the bedside or in the outpatient clinic with immediate results and good reproducibility. Limitations include failure in around 5% of cases, mainly in obese patients. So far, TE has been mostly validated in chronic hepatitis C, with diagnostic performance equivalent to that of serum markers for the diagnosis of significant fibrosis. Combining TE with serum markers increases diagnostic accuracy and as a result, liver biopsy could be avoided for initial assessment in most patients with chronic hepatitis C. This strategy warrants further evaluation in other etiological types of chronic liver diseases. TE appears to be an excellent tool for early detection of cirrhosis and

may have prognostic value in this setting. As TE has excellent patient acceptance it could be useful for monitoring fibrosis progression and regression in the individual case, but more data are awaited for this application. Guidelines are needed for the use of TE in clinical practice. This technology has been promoted as a noninvasive and painless alternative for a liver biopsy for monitoring liver health in patients with hepatitis.

Crossan et al. (2015) reviewed the cost-effectiveness of treating patients in the absence of liver biopsy using a variety of statistical models but generally found FibroScan was the most cost-effective tool. Patel and Wilder (2014) pointed to the high degree of accuracy by FibroScan for patients with cirrhosis but with the higher error rate by Metavir F2 or less.

In a prospective study, de Ledinghen et al (2006) evaluated the accuracy of liver stiffness measurement for the detection of fibrosis and cirrhosis in HIV/hepatitis C virus (HCV)-coinfected patients and compared its accuracy with other non-invasive methods. These researchers studied 72 consecutive HIV patients with chronic hepatitis C who had a simultaneous liver biopsy and liver stiffness measurement by transient elastography (FibroScan; Echosens, Paris, France) for the assessment of liver fibrosis. Liver stiffness values ranged from 3.0 to 46.4 kPa. Liver stiffness was significantly correlated to fibrosis stage (Kendall tau-b = 0.48; p < 0.0001). The area under the receiver operating characteristic (AUROC) curve of liver stiffness measurement was 0.72 for F > or = 2 and 0.97 for F = 4. For the diagnosis of cirrhosis, AUROC curves of liver stiffness measurement were significantly higher than those for platelet count (p = 0.02), aspartate aminotransferase/ALT ratio (p = 0.0001), Aspartate aminotransferase-to-Platelet Ratio Index (p = 0.01), and FIB-4 (p = 0.004). The authors concluded that liver stiffness measurement is a promising noninvasive method for the assessment of fibrosis in HIV-infected patients with chronic HCV infection. They also noted that its use for the follow-up of these patients should be further evaluated.

Foucher and colleagues (2006) assessed the accuracy of FibroScan for the detection of cirrhosis in patients with chronic liver disease. A total of 711 patients with chronic liver disease were studied. Etiologies of chronic liver diseases were hepatitis C virus or hepatitis B virus infection, alcohol, non-alcoholic steatohepatitis, other, or a combination of the above etiologies. Liver fibrosis was evaluated according to the METAVIR score. Stiffness was significantly correlated with fibrosis stage (r = 0.73, p < 0.0001). Areas under the receiver operating characteristic curve (95 % CI) were 0.80 (0.75 to 0.84) for patients with significant fibrosis (F > 2), 0.90 (0.86 to 0.93) for patients with severe fibrosis (F3), and 0.96 (0.94 to 0.98) for patients with cirrhosis. Using a cut off value of 17.6 kPa, patients with cirrhosis were detected with a positive predictive value and a NPV of 90 %. Liver stiffness was significantly correlated with clinical, biological, and morphological parameters of liver disease. With an NPV greater than 90 %, the cut off values for the presence of esophageal varices stage 2/3, cirrhosis Child-Pugh B or C, past history of ascites, hepatocellular carcinoma, and esophageal bleeding were 27.5, 37.5, 49.1, 53.7, and 62.7 kPa, respectively. The authors concluded that FibroScan is a promising non-invasive method for detection of cirrhosis in patients with chronic liver disease. They noted that its use for the follow-up and management of these patients could be of great interest and should be evaluated further.

Corpechot and associates (2006) assessed the diagnostic performance of liver stiffness measurement (LSM) for the determination of fibrosis stage in chronic cholestatic diseases. A total of 101 patients with primary biliary cirrhosis (PBC, n = 73) or primary sclerosing cholangitis (PSC, n = 28) were prospectively enrolled in a multi-center study. All patients underwent liver biopsy (LB) and LSM. Histological and fibrosis stages were assessed on LB by two pathologists. LSM was performed by FibroScan. Efficiency of LSM for the determination of histological and fibrosis stages were determined by a ROC curve analysis. Analysis failed in 6 patients (5.9 %) because of unsuitable LB (n = 4) or LSM (n = 2). Stiffness values ranged from 2.8 to 69.1 kPa (median of 7.8 kPa). LSM was correlated to both fibrosis (Spearman's rho = 0.84, p < .0001) and histological (0.79, p < .0001) stages. These correlations were still found when PBC and PSC patients were analyzed separately. Areas under ROC curves were 0.92 for fibrosis stage (F) > or = 2, 0.95 for F > or = 3

and 0.96 for F = 4. Optimal stiffness cutoff values of 7.3, 9.8, and 17.3 kPa showed F > or = 2, F > or = 3 and F = 4, respectively. LSM and serum hyaluronic acid level were independent parameters associated with extensive fibrosis on LB. The authors concluded that FibroScan is a simple and reliable non-invasive means for assessing biliary fibrosis. They stated that it should be a promising tool to assess anti-fibrotic therapies in PBC or PSC.

The Canadian Agency for Drugs and Technologies in Health (CADTH) performed an evaluation on FibroScan for non-invasive assessment of liver fibrosis (Murtagh and Foster, 2006). It stated that the diagnostic performance of FibroScan is good for identifying severe fibrosis or cirrhosis, but it is less accurate for milder presentations. It concluded that FibroScan is a promising technology, but large multi-center studies comparing a range of emerging non-invasive fibrosis staging technologies are needed. An earlier assessment by the French Committee for Evaluation and Diffusion of Innovative Technologies (CEDIT, 2004) reached similar conclusions, stating that the absence of conclusive evidence concerning the diagnostic value of FibroScan argues against its immediate dissemination. More recently, an assessment by the French National Authority for Health (HAS, 2007) concluded that additional studies are necessary to evaluate the comparative cost-effectiveness of different methods of assessing liver fibrosis (e.g., FibroTest, FibroScan, and biopsy). A technology assessment by the Malaysian Ministry of Health (Darus, 2008) reached similar conclusions about the need for additional research for the FibroScan.

de Franchis et al (2007) stated that transient elastography (FibroScan) might be of value for the non-invasive diagnosis of cirrhosis; however, its reproducibility needs to be further validated. Furthermore, Berrutti et al (2007) noted that FibroScan is a new, non-invasive method to evaluate liver stiffness and, consequently, the degree of liver fibrosis. Since its use in the clinical setting is of great interest, further studies should define the exact role of this procedure.

It has been noted that the test is not recommended for people with pacemakers or for pregnant women, and inaccurate or unobtainable readings are more common in people who are obese, older, have ascites (a build-up of fluid between the abdominal wall and organs) or have features of metabolic syndrome (Kemp, W. & Roberts 2013). This is due to the fact that the FibroScan technique requires adequate visualization of the liver to obtain readings. Being obese or with the presence of ascites, the vibration wave cannot penetrate resulting in unreliable or failure of readings.

Acoustic Radiation Force Impulse Elastography (AFRI) is an ultrasound test that utilizes a probe to produce an acoustic push pulse, which generates shear waves that propagate in tissue to assess liver stiffness. This test evaluates the wave propagation speed to assess liver stiffness, the faster the shear wave speed, the harder the object.

Serum fibrosis biomarkers consists of direct and indirect serum testing and risk scoring based on combining indirect and direct markers. The American Association of Liver Disease and the Infectious Disease Society of American published an update in September 2015 of the practice guidance for testing, managing and treating adults infected with hepatitis C. The recommendation for staging patients with chronic liver disease states: "The most efficient approach to fibrosis assessment is to combine direct biomarkers and vibration controlled transient liver elastography".

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