

Date: December 16, 2016

Subject: Changes to treatment guidance for chronic Hepatitis C virus (HCV) infection

Effective January 1, 2017, Centennial Care MCOs are directed to approve properly requested treatments for the following Centennial Care members with chronic HCV infection:

1. All members over age 17, all HCV genotypes, with F1 level or greater of fibrosis (or equivalent):
 - a. APRI (using 40 as the upper normal limit for AST) score greater than or equal to 0.3^{1,2,3} (F1 equivalent), **OR**
 - b. FIB-4 greater than or equal to 1.29^{4,5,7} (F1 equivalent), **OR**
 - c. Transient elastography (Fibroscan®) score greater than or equal to 5.0 kPa^{6,7} (F1 equivalent), **OR**
 - d. Liver biopsy confirming a METAVIR score F1 or greater, **OR**
 - e. Imaging study that shows cirrhosis, **OR**
 - f. FibroSure®/FibroTest score of greater than or equal to 0.27⁸ (F1 equivalent) OR Fibrometer with greater than or equal to F1 predominance
2. Specifically, all those with decompensated cirrhosis (jaundice, ascites, variceal bleeding, hepatic encephalopathy, spontaneous bacterial peritonitis, or Child-Pugh class B or C) and/or hepatocellular carcinoma should be treated unless the requesting physician certifies that the patient's life expectancy is < 12 months
3. All patients with these extrahepatic manifestations of HCV infection should be treated:
 - a. Type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations (e.g. vasculitis), or
 - b. Kidney disease (proteinuria, nephrotic syndrome or glomerulonephritis)
4. Other high-risk populations that should also be treated:
 - a. Pre- and post-liver transplant, or other solid organ transplant
 - b. HIV-1 or Hepatitis B co-infection
 - c. Type 2 diabetes mellitus (insulin resistant)

- d. Debilitating fatigue impacting quality of life (e.g., secondary to extra-hepatic manifestations and/or liver disease) as documented in chart notes as being chronic and persistent and still present over prior six months
 - e. Porphyria cutanea tarda
 - f. Men who have sex with men, with high-risk sexual practices
 - g. Active injection drug users
 - h. Patients on long-term hemodialysis
 - i. Women of childbearing age who wish to get pregnant
 - j. HCV-infected health care workers who perform exposure-prone procedures
5. Note that in all cases, MCOs are directed to ensure (using the AASLD/IDSA guidelines) that each treatment request is appropriate with respect to:
- a. HCV genotype and viral load
 - b. Drug dose(s) and duration(s). Note that the MCOs preferred formulary agent may be given preference if the level of evidence and effectiveness (as measured by SVR) is equal or greater, and no drug interactions are of concern
 - c. The presence or absence of advanced fibrosis or cirrhosis. For the purpose of making treatment decisions using the AASLD/IDSA guidance, “cirrhosis” can be considered to be present if any of the following are present:
 - i. APRI ≥ 1.0 ⁹
 - ii. Fib-4 ≥ 3.25 ¹⁰
 - iii. Liver biopsy confirming a METAVIR Score of F4
 - iv. Transient Elastography Score ≥ 12.5 kP¹¹ (F4 equivalent)
 - v. Fibrotest ≥ 0.73 ¹² (F4 equivalent) OR Fibrometer with F4 predominance
 - vi. Radiographic imaging or physical exam findings consistent with cirrhosis
 - d. Prior HCV treatment experience.
 - i. Plans may require resistance-associated variants (RAVs) testing, based on AASLD guidance
6. MCOs shall, by March 31, 2017, contact members (and their requesting providers) who now meet the above treatment criteria, but were previously denied treatment, for reconsideration of their HCV treatment requests. Also, by June 30, 2017, submit a report to MAD documenting the results of this process.
7. MCOs are directed to work to expedite the handling of all treatment requests using the “Uniform New Mexico HCV Checklist for Centennial Care” (attached). The header of this form may be adapted to make it specific to your organization.
8. Guidance regarding lost or stolen medications:

- a. MCOs are directed to use the same criteria currently used for refills of other lost or stolen medications
- b. MCOs are directed to use Care Coordination and other functions to minimize this occurrence (see below)
9. Guidance regarding requests for off-label, experimental, and other forms of treatment that are not specified in the guidelines
 - a. MCOs are directed to initiate a peer to peer consultation with the requesting physician to further understand the request and its rationale
 - b. MCOs are directed to present the case to Project ECHO before issuing a denial
10. Note that a “properly requested treatment” as defined above means that:
 - a. The checklist form is completed fully as directed and submitted
 - b. Necessary lab data and copies of medical records are attached
 - c. The requested drug(s), dose(s), and length of treatment match the genotype and is/are consistent with AASLD/IDSA guidance as written (the level of evidence in the guidance should not be considered relevant to length of treatment decisions)
11. MCOs are granted the option to expand their treatment criteria beyond these guidelines, with advance notice to and approval by the Medical Assistance Division.

MCOs are directed to:

1. Not use active alcohol or drug use as screening criteria for treatment approval or denial
2. Not use the specialty of the requesting provider as screening criteria for treatment approval or denial. If an MCO receives multiple requests from a provider that are not genotype-drug-length of treatment appropriate, the provider should be encouraged to use Project ECHO.
3. Refer all members to a community health worker, care coordinator, or MCO specialty pharmacist at the time of drug treatment **request** in order to:
 - a. Make verbal contact directly with the member
 - b. Help expedite obtaining and submitting all necessary studies for an authorization decision
 - c. Help explain the Plan’s decision to the member
 - d. Help coordinate receipt of medications and enhance treatment adherence
 - Note that these treatment functions can be performed by, or in concert with, other Plan-contracted care coordination efforts (e.g., PBM or drug manufacturer)
 - Any member with both chronic HCV infection *and* liver fibrosis at the F1 level or above will be considered to meet the criterion of “comorbid condition” until treatment is completed and SVR is achieved (Centennial Care contract section 4.4.6.1.1.)

- Also, per section 4.4.4.1.1 of the Centennial Care contract, any member with chronic HCV infection who does not meet treatment criteria must be managed at a minimum of Care Coordination level 1 with quarterly review of claims and utilization data.
- 4. Submit monthly data concerning number of requests, approvals, and denials by fibrosis stage (or equivalent) and genotype for all member treatment requests. MAD will supply revised spreadsheets for completion. Note that this will require each MCO to effectively stage each patient at the time of each treatment request, by working to ensure the completeness of data submitted. Patients with the above listed extrahepatic manifestations need not be staged further as they will be treated and can be counted in the “Extrahepatic Manifestations” category.
- 5. Send a representative to attend quarterly meetings with other MCOs and representatives of MAD as part of a HCV Workgroup to review current data and recent guidance revisions and propose evidence-based future revisions to treatment guidelines.
- 6. Continue to implement a comprehensive plan of outreach to the Plan’s top five referring provider groups requesting oral drug treatment for chronic HCV-infected patients, including:
 - a. Attending an all-MCO workgroup to define a common “Hepatitis C Treatment Packet,” whose purpose is to recruit, educate and assist new providers in treating Hepatitis C in their patients
 - b. A plan to educate providers on the use of the revised “Uniform New Mexico HCV Checklist for Centennial Care” (attached)
 - c. Clarification of new treatment guidelines
 - d. Clarification of prior authorization processes
 - e. Use of Project ECHO review for:
 - i. Any provider needing assistance on any case, and
 - ii. All cases for which retreatment (after prior all-oral therapy) is being requested and the MCO feels such a review would benefit the member
- 7. Continue to implement a comprehensive plan to expand HCV screening efforts to conform to USPSTF/CDC/AASLD/IDSA guidelines (listed below), including:
 - a. Outreach to contracted providers
 - b. Outreach to members who are recommended for screening
 - c. Collaboration with contracted laboratories to aid in case identification
 - d. Guidelines for screening:
 - i. One-time HCV testing is recommended for persons born between 1945 and 1965, without prior ascertainment of risk.
 - ii. Other persons should be screened for risk factors for HCV infection, and one-time testing should be performed for all persons with behaviors, exposures, and conditions associated with an increased risk of HCV infection.

1. *Risk behaviors*
 - a. Injection-drug use (current or ever, including those who injected once)
 - b. Intranasal illicit drug use
2. *Risk exposures*
 - a. Long-term hemodialysis (ever)
 - b. Getting a tattoo in an unregulated setting
 - c. Healthcare, emergency medical, and public safety workers after needle sticks, sharps, or mucosal exposures to HCV-infected blood
 - d. Children born to HCV-infected women
 - e. Prior recipients of transfusions or organ transplants, including persons who:
 - i. were notified that they received blood from a donor who later tested positive for HCV infection
 - ii. received a transfusion of blood or blood components, or underwent an organ transplant before July 1992
 - iii. received clotting factor concentrates produced before 1987
 - iv. Persons who were ever incarcerated
 - f. Other
 - i. HIV infection
 - ii. Unexplained chronic liver disease and chronic hepatitis including elevated alanine aminotransferase levels
 - iii. Solid organ donors

¹ Holmberg SD, Gordon SC, *et al.* Noninvasive Serum Fibrosis Markers for Screening and Staging Chronic Hepatitis C Virus Patients in a Large US Cohort. *CID* 2013;57:243. Table 2. Lower limit of 95% confidence intervals used for APRI and FIB-4 scoring at F2 level.

² Amorim TG, Staub GJ, Lazzarotto C, Silva AP, Manes J, Ferronato Mda G, Shiozawa MB, Narciso-Schiavon JL, Dantas-Correa EB, Schiavon Lde L. Validation and comparison of simple noninvasive models for the prediction of liver fibrosis in chronic hepatitis C. *Ann Hepatol.* 2012 Nov-Dec;11(6):855-61.

³ Loeza-del-Castillo A, Paz-Pineda F, Oviedo-Cárdenas E, Sánchez-Avila F, Vargas-Vorácková F. AST to platelet ratio index (APRI) for the noninvasive evaluation of liver fibrosis. *Ann Hepatol.* 2008 Oct-Dec;7(4):350-7.

⁴ de Oliveira AC, El-Bacha I, Vianna MV, Parise ER. Utility and limitations of APRI and FIB4 to predict staging in a cohort of nonselected outpatients with hepatitis C. *Ann Hepatol.* 2016 May-Jun;15(3):326-32.

⁵ Holmberg, *op. cit.*

⁶ Foucher J, de Ledhingen V. Diagnosis of cirrhosis by transient elastography (FibroScan): a prospective study. *Gut*, 2006;55(3):405. Table 2. 90% predictive value score used.

⁷ van du Putte DF, van Erpecum K, *et al.* Impact of Fibroscan® on management of chronic viral hepatitis in clinical practice. *Ann Hepatology*, 2011; 10(4): 469-476. See page 470, column b.

⁸ Rossi E, Jeffrey G, *et al.* Validation of the FibroTest Biochemical Markers Score in Assessing Liver Fibrosis in Hepatitis C Patients. *Clinical Chemistry*, 2003;49(3):450–454.

⁹ Lin ZH, Xin YN, Dong QJ, *et al.* Performance of the aspartate aminotransferase-to-platelet ratio index for the staging of hepatitis C-related fibrosis: an updated meta-analysis. *Hepatology*. 2011;53:726-36. In a meta-analysis of 40 studies, investigators concluded that an APRI score greater than 1.0 had a sensitivity of 76% and specificity of 72% for predicting cirrhosis. In addition, they concluded that APRI score greater than 0.7 had a sensitivity of 77% and specificity of 72% for predicting significant hepatic fibrosis. See APRI calculator at www.hepatitisc.uw.edu (click on Clinical Calculators tab and then APRI Calculator). Note also that this is the numeric threshold used by NM Project ECHO.

¹⁰ Sterling RK, Lissen E, Clumeck N, *et al.* Development of a simple noninvasive index to predict significant fibrosis patients with HIV/HCV co-infection. *Hepatology* 2006;43:1317-1325. Using a lower cutoff value of 1.45, a FIB-4 score <1.45 had a negative predictive value of 90% for advanced fibrosis (Ishak fibrosis score 4-6 which includes early bridging fibrosis to cirrhosis). In contrast, a FIB-4 >3.25 would have a 97% specificity and a positive predictive value of 65% for advanced fibrosis. In the patient cohort in which this formula was first validated, at least 70% patients had values <1.45 or >3.25. See FIB-4 calculator at www.hepatitisc.uw.edu. Click on Clinical Calculators and then FIB-4 Calculator. Note also that this is the numeric threshold used by NM Project ECHO.

¹¹ van du Putte, *op. cit.* See page 470, column b.

¹² Rossi E, Jeffrey G, *et al.* Validation of the FibroTest Biochemical Markers Score in Assessing Liver Fibrosis in Hepatitis C Patients. *Clinical Chemistry*, 2003;49(3):450–454.