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MEMORANDUM

MEMO NO.
QI-2227 [Replaces QI 1829]
FFS 22-08 [Replaces FFS 18-10]

TO: Medicaid Fee-For-Service (FFS), QUEST Integration (QI) Health Plans, Providers, and Pharmacies

FROM: Judy Mohr Peterson, PhD JMP
Med-QUEST Division Administrator

Curtis Toma MD CT
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SUBJECT: DIRECT ACTING ANTIVIRAL (DAA) MEDICATIONS FOR TREATMENT OF CHRONIC HEPATITIS C INFECTION

This memorandum is an update to QI-1829 and serves as broad guidance to the QI health plans for the treatment of chronic hepatitis C virus (HCV) infection. Over 2 million adults in the United States have hepatitis C virus (HCV) infection, and it contributes to approximately 14,000 deaths a year. Eight to 12 weeks of highly effective direct-acting antiviral (DAA) treatment, which can cure ≥ 95% of cases, is recommended for persons with hepatitis C.[1] The Centers for Disease Control and Prevention (CDC) has reported that Medicaid beneficiaries are less likely to be treated for hepatitis C than patients covered by Medicare or commercial insurance.[1] This has bearing on health outcomes for the Med-QUEST population, since HCV is one of the leading causes of liver cancer in Hawai'i [2] and is also associated with lower life expectancy compared to the rest of the state.

Medicaid coverage of chronic HCV treatment with DAA medications should be covered in accordance with the following Medicaid FFS guidelines. QI health plan policies for the coverage of chronic HCV

DAA medications shall not be more restrictive than the Medicaid FFS guidelines. The guiding principles for the state guidelines are twofold. First, to follow best practice guidelines. Currently, the national best practice guidelines are from the joint American Association of Liver Disease (AASLD) – Infectious Disease Society of America (IDSA) HCV Guidance: Recommendations for Testing, Managing and Treating Hepatitis C. Second, to provide consistency across the QI health plans for the coverage of HCV DAA's. The following are the updated guidelines for the coverage of HCV DAA's.

1) Treatment is in accordance with FDA-approved guidelines.

2) Treatment is in accordance with the national best practice guidelines which are best exemplified by the joint AASLD – IDSA HCV Guidance: Recommendations for Testing, Managing and Treating Hepatitis C (www.hcvguidelines.org). MQD will cover the treatment regimens as recommended in AASLD-IDSA HCV Guidance.

3) Providers should continue to work closely with patients to address any issues affecting compliance. Good compliance and completion of a treatment course is essential for eradicating Hepatitis C. However, alcohol use and substance abuse are not contraindications to DAA therapy.

4) Patients with chronic HCV can be treated at any stage. There are no treatment restrictions in terms of fibrosis stage.

5) In alignment with the AASLD-IDSA HCV Guidance, a small minority of patients with medical complexities may be better served by specialists. Patients requiring specialized care, including but are not limited to conditions below, should have DAA treatment directed by or in collaboration with a specialist or transplant facility to assist with complexity of care.

    a. Patients with decompensated cirrhosis
    b. Patients with hepatocellular carcinoma
    c. Patients who are candidates for liver transplantation or other solid organ transplantation
    d. Patients who develop recurrent HCV infection post liver transplantation
    e. Patients with End Stage Renal Disease (ESRD, GFR < 30)
    f. Patients with history of solid organ transplantation on immunosuppressive therapy
    g. Patients with acute HCV infection
    h. Patients with coinfection with HBV/HCV and/or HIV/HCV
    i. Patients with history of prior hepatitis C treatment failure
    j. HCV in pregnancy and in children

6) The majority of patients with hepatitis C do not have the medical complexities listed above and have the option to be treated by primary care providers. These include treatment

naïve patients without cirrhosis and treatment naïve patients with compensated cirrhosis. Patients with decompensated cirrhosis would be an example of medical complexity better served by a specialist per AASLD-IDSA guidelines. Refer to Appendix A for the AASLD- IDSA simplified summary of the national guidelines for HCV treatment and to www.hcvguidance.org for complete guidance.

MQD will work closely with the QI health plans on a process to approve primary care providers and provide consistency among the QI health plans. Qualified providers include but are not limited to those who complete the Hepatitis C Echo series and/or work in collaboration with a specialist. In addition, primary care providers who do not meet above can request to become approved providers. Specialists such as HIV specialists, hepatologists, gastroenterologists, and infectious disease also continue as qualified prescribers.

7) Medicaid formularies must include the treatment regimens recommended by AASLD-IDSA HCV Guidance. The QI health plans may not restrict access to a recommended treatment regimen in lieu of individual QI plan formulary alternative not listed as a treatment regimen in the AASLD-IDSA HCV Guidance.

8) The goal of this HCV policy is to assure adherence to the best practice guidance, currently outlined by the AASLD-IDSA HCV Guidance. For treatment regimens following the AASLD-IDSA HCV Guidance, there will be no prior authorization.

Please contact Dr. Curtis Toma, Medical Director, at (808) 692-8106 or via e-mail at ctoma@dhs.hawaii.gov should you have any questions.

References:

1) Thompson WW, Symum H, Sandul A, et al. Vital Signs: Hepatitis C Treatment Among Insured Adults — United States, 2019–2020. *MMWR Morb Mortal Wkly Rep.* 2022;71:1011- 1017. DOI: http://dx.doi.org/10.15585/mmwr.mm7132e1.
2) Wong L, Ogihara M, Ji J, Tsai N. Changing characteristics of hepatocellular cancer in Hawaii over time. *American Journal of Surgery*. 2015;210(1):146-152.
3) Ly KN, Miniño AM, Liu SJ, et al. Deaths Associated With Hepatitis C Virus Infection Among Residents in 50 States and the District of Columbia, 2016–2017. *Clinical Infectious Diseases*. 2020;71(5):1149-1160. https://doi.org/10.1093/cid/ciz976
4) American Association for The Study of Liver Disease Treatment (AASLD) and Infectious Disease Society of America (IDSA) HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C [updated October 24, 2022]. http://hcvguidelines.org; accessed December 12, 2022.
5) Food and Drug Administration. www.FDA.gov; accessed December 12, 2022.
6) Stephenson J. Too Few People with Hepatitis C Receive Timely Curative Treatment. *JAMA Health Forum.* 2022;3(8):e223414. doi:10.1001/jamahealthforum.2022.341

Appendix A

Simplified HCV Treatment Algorithm for Treatment-Naive Adults Without Cirrhosis Simplified HCV Treatment Algorithm for Treatment-Naive Adults With Compensated Cirrhosis

Simplified HCV Treatment Algorithm for Treatment-Naive Adults Without Cirrhosis

WHO IS ELIGIBLE FOR SIMPLIFIED TREATMENT

Adults with chronic hepatitis C (any genotype)
who do not have cirrhosis
and have not previously received hepatitis C treatment

WHO IS *NOT* ELIGIBLE FOR SIMPLIFIED TREATMENT

Patients who have any of the following characteristics:

- Prior hepatitis C treatment
- Cirrhosis (see simplified treatment for treatment-naive adults with compensated cirrhosis)
- HIV or HBsAg positive
- Current pregnancy
- Known or suspected hepatocellular carcinoma
- Prior liver transplantation

PRETREATMENT ASSESSMENT *

- **Calculate FIB-4 score.**
- **Cirrhosis assessment**: Liver biopsy is not required. For the purpose of this guidance, a patient is presumed to have cirrhosis if they have a FIB-4 score >3.25 **or** any of the following findings from a previously performed test.
  - Transient elastography indicating cirrhosis (eg, FibroScan stiffness >12.5 kPa)
  - Noninvasive serologic tests above proprietary cutoffs indicating cirrhosis (eg, FibroSure, Enhanced Liver Fibrosis Test, etc)
  - Clinical evidence of cirrhosis (eg, liver nodularity and/or splenomegaly on imaging, platelet count <150,000/mm^3, etc)
  - Prior liver biopsy showing cirrhosis
- **Medication reconciliation:** Record current medications, including over-the-counter drugs, and herbal/dietary supplements.
- **Potential drug-drug interaction assessment:** Drug-drug interactions can be assessed using the AASLD/IDSA guidance or the University of Liverpool drug interaction checker.
- **Education:** Educate the patient about proper administration of medications, adherence, and prevention of reinfection.
- **Pretreatment laboratory testing**

  Within 6 months of initiating treatment:
  - Complete blood count (CBC)
  - Hepatic function panel (ie, albumin, total and direct bilirubin, alanine aminotransferase [ALT], and aspartate aminotransferase [AST])
  - Calculated glomerular filtration rate (eGFR)

  Any time prior to starting antiviral therapy:
  - Quantitative HCV RNA (HCV viral load)
  - HIV antigen/antibody test
  - Hepatitis B surface antigen

  Before initiating antiviral therapy:
  - Serum pregnancy testing and counseling about pregnancy risks of HCV medication should be offered to women of childbearing age.

RECOMMENDED REGIMENS*

Glecaprevir (300 mg) / pibrentasvir (120 mg)
taken with food for a duration of 8 weeks

Sofosbuvir (400 mg) / velpatasvir (100 mg)
for a duration of 12 weeks

ON-TREATMENT MONITORING

- Inform patients taking diabetes medication of the potential for symptomatic hypoglycemia. Monitoring for hypoglycemia is recommended
- Inform patients taking warfarin of the potential for changes in their anticoagulation status. Monitoring INR for subtherapeutic anticoagulation is recommended.
- No laboratory monitoring is required for other patients.
- An in-person or telehealth/phone visit may be scheduled, if needed, for patient support, assessment of symptoms, and/or new medications.

POST-TREATMENT ASSESSMENT OF CURE (SVR)

- Assessment of quantitative HCV RNA and a hepatic function panel are recommended 12 weeks or later following completion of therapy to confirm HCV RNA is undetectable (virologic cure) and transaminase normalization.
- Assessment for other causes of liver disease is recommended for patients with elevated transaminase levels after achieving SVR.

FOLLOW-UP AFTER ACHIEVING VIROLOGIC CURE (SVR)

- No liver-related follow-up is recommended for noncirrhotic patients who achieve SVR.
- Patients with ongoing risk for HCV infection (eg, intravenous drug use or MSM engaging in unprotected sex) should be counseled about risk reduction, and tested for HCV RNA annually and whenever they develop elevated ALT, AST, or bilirubin.
- Advise patients to avoid excess alcohol use.

FOLLOW-UP FOR PATIENTS WHO DO *NOT* ACHIEVE A VIROLOGIC CURE

- Patients in whom initial HCV treatment fails to achieve cure (SVR) should be evaluated for retreatment by a specialist, in accordance with AASLD/IDSA guidance.
- Until retreatment occurs, assessment for disease progression every 6 to 12 months with a hepatic function panel, CBC, and INR is recommended.
- Advise patients to avoid excess alcohol use.

AASLD

*More detailed descriptions of the patient evaluation process and antivirals used for HCV treatment, including the treatment of patients with cirrhosis, can be found at www.hcvguidelines.org. Updated: August 27, 2020

IDSA Infectious Diseases Society of America

Simplified HCV Treatment Algorithm for Treatment-Naive Adults With Compensated Cirrhosis

WHO IS *NOT* ELIGIBLE FOR SIMPLIFIED TREATMENT

Patients who have any of the following characteristics:

- **Current or prior** episode of decompensated cirrhosis, defined as Child-Turcotte-Pugh (CTP) score ≥7 (ascites, hepatic encephalopathy, total bilirubin >2.0 mg/dL, albumin ≤3.5 g/dL, or INR ≥1.7)
- Prior hepatitis C treatment
- End-stage renal disease (ie, eGFR <30 mL/min/m^2) (see Patients with Renal Impairment section)
- HIV or HBsAg positive
- Current pregnancy
- Known or suspected hepatocellular carcinoma
- Prior liver transplantation

(See HCV guidance for treatment recommendations for these patients.)

WHO IS ELIGIBLE FOR SIMPLIFIED TREATMENT

- Adults with chronic hepatitis C (any genotype) who have compensated cirrhosis (Child-Pugh A) and have not previously received hepatitis C treatment
- Liver biopsy is not required. For the purpose of this guidance, a patient is presumed to have cirrhosis if they have a FIB-4 score >3.25 **or** any of the following findings from a previously performed test.
  - Transient elastography indicating cirrhosis (eg, FibroScan stiffness >12.5 kPa)
  - Noninvasive serologic tests above proprietary cutoffs indicating cirrhosis (eg, FibroSure, Enhanced Liver Fibrosis Test, etc)
  - Clinical evidence of cirrhosis (eg, liver nodularity and/or splenomegaly on imaging, platelet count <150,000/mm^3, etc)
  - Prior liver biopsy showing cirrhosis

PRETREATMENT ASSESSMENT *

- **Calculate FIB-4 score.**
- **Calculate CTP score:** Patients with a CTP score ≥7 (ie, CTP B or C) have decompensated cirrhosis and this simplified treatment approach is not recommended.
- **Ultrasound of the liver** (conducted within the prior 6 months): Evaluate to exclude HCC and subclinical ascites.
- **Medication reconciliation**: Record current medications, including over-the-counter drugs and herbal/dietary supplements.
- **Potential drug-drug interaction assessment:** Drug-drug interactions can be assessed using the AASLD/IDSA guidance or the University of Liverpool drug interaction checker.
- **Education:** Educate the patient about proper administration of medications, adherence, and prevention of reinfection.
- **Pretreatment laboratory testing** (see next column)

Within 3 months of initiating treatment

- Complete blood count (CBC)
- International normalized ratio (INR)
- Hepatic function panel (ie, albumin, total and direct bilirubin, alanine aminotransferase [ALT], and aspartate aminotransferase [AST])
- Calculated glomerular filtration rate (eGFR)

Any time prior to starting antiviral therapy

- Quantitative HCV RNA (HCV viral load)
- HIV antigen/antibody test
- Hepatitis B surface antigen
- HCV genotype (if treating with sofosbuvir/velpatasvir)

Before initiating antiviral therapy

- Serum pregnancy testing and counseling about pregnancy risks of HCV medication should be offered to women of childbearing age.

RECOMMENDED REGIMENS*

Genotype 1-6:
Glecaprevir (300mg)/pibrentasvir (120 mg) taken with food for a duration of 8 weeks

Genotype 1, 2, 4, 5, or 6:
Sofosbuvir (400 mg)/velpatasvir (100 mg) for a duration of 12 weeks

NOTE: Patients with genotype 3 require baseline NS5A resistance-associated substitution (RAS) testing. Those without Y93H can be treated with 12 weeks of sofosbuvir/velpatasvir. If Y93H is present, see HCV guidance for treatment recommendations.

ON-TREATMENT MONITORING

- Providers may order blood tests to monitor for liver injury during treatment because hepatic decompensation (eg, jaundice, etc) occurs rarely among patients with cirrhosis receiving HCV antiviral treatment.
- Patients should see a specialist if they develop worsening liver blood tests (eg, bilirubin, AST, ALT, etc); jaundice, ascites, or encephalopathy; or new liver-related symptoms.
- Inform patients taking diabetes medication of the potential for symptomatic hypoglycemia. Monitoring for hypoglycemia is recommended.
- Inform patients taking warfarin of the potential for changes in their anticoagulation status. Monitoring INR for subtherapeutic anticoagulation is recommended.
- An in-person or telehealth/phone visit may be scheduled, if needed, for patient support, assessment of symptoms, and/or new medications.

POST-TREATMENT ASSESSMENT OF CURE (SVR)

- Assessment of quantitative HCV RNA and a hepatic function panel are recommended 12 weeks or later following completion of therapy to confirm HCV RNA is undetectable (virologic cure) and transaminase normalization.
- Assessment for other causes of liver disease is recommended for patients with elevated transaminase levels after achieving SVR.

FOLLOW-UP AFTER ACHIEVING VIROLOGIC CURE (SVR)

- Ultrasound surveillance for HCC (with or without alpha-fetoprotein testing) every 6 months is recommended for patients with cirrhosis in accordance with AASLD guidance.
- Upper endoscopic surveillance for esophageal varices is recommended in accordance with AASLD guidance on portal hypertensive bleeding in cirrhosis
- Patients with ongoing risk for HCV infection (eg, IV drug use or MSM engaging in unprotected sex) should be counseled about risk reduction, and tested for HCV RNA annually and whenever they develop elevated ALT, AST, or bilirubin.
- Patients should abstain from alcohol to avoid progression of liver disease.

FOLLOW-UP FOR PATIENTS WHO DO *NOT* ACHIEVE A VIROLOGIC CURE

- Patients in whom initial HCV treatment fails to achieve cure (SVR) should be evaluated for retreatment by a specialist, in accordance with AASLD/IDSA guidance.
- Ultrasound surveillance for hepatocellular carcinoma (with or without alpha-fetoprotein testing) every 6 months is recommended for patients with cirrhosis, in accordance with AASLD guidance.
- Assessment for disease progression every 6 to 12 months with a hepatic function panel, CBC, creatinine, and INR is recommended.
- Patients should abstain from alcohol to avoid progression of liver disease.

AASLD

* More detailed descriptions of the patient evaluation process and antivirals used for HCV treatment can be found at www.hcvguidelines.org.

IDSA