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June 3, 2015

MEMORANDUM

MEMO NO.
QI-1510

TO: QUEST Integration Health Plans

FROM: Leslie K. Tawata
Acting Med-QUEST Division Administrator

SUBJECT: HEPATITIS C MEDICATION COVERAGE GUIDELINES

This memorandum replaces the following memoranda: ADM-1408, ADMX-1408, QI-1411, and QI-1411A. Act 20 signed into law by Governor David Ige on April 23, 2015, allows Medicaid managed care medical plans to prior authorize Hepatitis C medications for individuals enrolled in a Medicaid managed care plan. Attached is the Med-QUEST Division coverage guideline on medications for the treatment of Hepatitis C for QUEST Integration health plans.

Health plans shall use these guidelines in prior authorizing medications for the treatment of Hepatitis C. These guidelines may be updated as more evidence and other treatments become available.

Please contact Dr. Curtis Toma via e-mail at ctoma@medicaid.dhs.state.hi.us or call him at 692-8106 should you have any questions.

Attachment

Direct Acting Antiviral Medications for Treatment of Chronic Hepatitis C Infection

Treatment of chronic Hepatitis C virus (HCV) infection with direct acting antiviral (DAA) medications may be covered when all of the following inclusion criteria are met (subject to limitations/exclusions).

1) Patient is at least 18 years of age.

2) Treatment is in accordance with Food and Drug Administration (FDA) approved treatment regimens for each genotype (currently limited to HCV genotype 1, 2, 3 and 4) and subtype, when applicable (Appendix A).

3) Patient has chronic HCV infection and a baseline quantitative HCV ribonucleic acid (RNA) result within the previous 3 months of starting treatment.

4) Patient has at least one of the following criteria:
    a. Liver biopsy with a metavir score of F3 or F4.
    b. Transient elastography (Fibroscan) greater than or equal to 9.5 kPa.
    c. Radiologic imaging consistent with cirrhosis (e.g., evidence of portal hypertension).
    d. Clinical evidence of cirrhosis such as ascites, portal hypertension or esophageal varices.
    e. Serious extrahepatic manifestations of Hepatitis C, such as cryoglobulinemia.
    f. Patient is an active candidate for liver transplantation (Appendix B).

5) The medication is being prescribed by, or in consultation with, one of the following specialists:
    a. Hepatologist,
    b. Gastroenterologist, or
    c. Infectious Disease Specialist.

6) Patient does not have a history of alcohol or other substance abuse within the 6 months prior to treatment as evidenced by history and urine toxicology screen.

7) Prescribing physician attests that the patient is at low risk for non-compliance.

8) Patient demonstrates good compliance and agrees to the following:
    a. 100% medication compliance.
    b. Regular follow up with specialty pharmacy, treating providers, and laboratory blood draws, such as HCV RNA levels, when ordered.
    c. No alcohol or illicit drug use during the course of treatment.
    d. Compliant with drug screening such as urine toxicology screen when ordered by provider.

9) Medical conditions that may impact adherence, including mental health conditions, must be well controlled prior to starting treatment as compliance is crucial to success.

DAA medications may be covered when all of the inclusion criteria specified previously are met (subject to limitations below). DAA medications may not be covered when any one of the following limitations/exclusions below is present:

1) End stage renal disease on hemodialysis.

2) Chronic decompensated liver disease as defined by Child-Pugh > 6, with exception for a patient who is an active candidate for liver transplantation (Appendix C).

3) Hepatocellular carcinoma, with exception for a patient who meets Milan criteria and is an active candidate for liver transplantation (Appendix B).

4) Contraindication to medications used in combination with DAA, including absolute contraindications to PEG- interferon or ribavirin (Appendix D).

Other considerations:

1) Avoid concurrent use of medications or supplements that are FDA contraindicated (Appendix E).

2) Patients who have coinfection with HCV/HBV should have HBV well controlled prior to starting treatment.

3) Patients who have coinfection with HCV/HIV will require close follow up with an infectious disease specialist.

4) In patients who have a history of solid organ transplantation, treatment with DAA may be contraindicated and consultation with transplant center should occur prior to starting treatment.

5) Other life threatening medical conditions, such as metastatic cancer, should be treated and controlled prior to starting CHC therapy with DAA medications.

Appendix A: Food and Drug Administration Approved Direct Acting Antiviral Treatments for Chronic Hepatitis C Virus Infection

Table 1: History of FDA approved DAA for the treatment of chronic Hepatitis C

Medication	FDA Approval Date
teleprevir (Incivek)	May 2011
boceprevir (Victrelis)	May 2011
simeprevir (Olysio)	November 2013
sofosbuvir (Sovaldi)	December 2013
sofosbuvir / ledipasvir (Harvoni)	October 2014
simeprevir / sofosbuvir (Olysio/Sovaldi)	November 2014
ombitasvir/paritaprevir/ritonavir with dasabuvir (Viekira Pak)	December 2014

Table 2: Summary of FDA Approved DAA HCV Treatments

Genotype	Cirrhosis Status	Treatment	Duration (weeks)
1	- Cirrhotic	ledipasvir / sofosbuvir (Harvoni) OR ombitasvir / paritaprevir / ritonavir + dasabuvir (Viekira Pak) GT 1a add ribavirin. GT 1b no ribavirin OR sofosbuvir (Sovaldi) + simeprevir (Olysio)	12 * 12 12
1	+ Cirrhotic	ledipasvir / sofosbuvir (Harvoni) Treatment naïve Treatment experienced OR ombitasvir / paritaprevir / ritonavir + dasabuvir (Viekira Pak) GT 1a GT 1b OR sofosbuvir (Sovaldi) + simeprevir (Olysio)	12-24 12 24 12-24 24 12 24
2	+/- Cirrhotic	sofosbuvir (Sovaldi) + ribavirin	12
3	+/- Cirrhotic	sofosbuvir (Sovaldi) + ribavirin	24
4	+/- Cirrhotic	sofosbuvir (Sovaldi) + PEG interferon + ribavirin	12

*HARVONI for 8 weeks can be considered in treatment-naïve patients without cirrhosis who have pretreatment HCV RNA less than 6 million IU/ml.

The FDA approved treatment regimens above are recommended in national guidelines including The American Association for The Study of Liver Disease Treatment (AASLD): Recommendations for Testing, Managing, and Treating Hepatitis C, updated on April 8, 2015 and the Department of Veterans Affairs National Hepatitis C Resource Center Program and the Office of Public Health (VA): Chronic Hepatitis C Virus (HCV) Infection: Treatment Considerations, updated on February 17, 2015. Accessed April 2015.

Table 3: FDA Approved HCV Treatment with Sofosbuvir (SOVALDI)

Genotype	Treatment	Duration(wks)
1	SOVALDI + peg interferon alfa (IF) + ribavirin	12
1	IF ineligible, SOVALDI + ribavirin	24
2	SOVALDI + ribavirin	12
3	SOVALDI + ribavirin	24
4	SOVALDI + IF + ribavirin	12

Table 4: FDA Approved HCV Treatment with Sofosbuvir / Ledipasvir (HARVONI)

Genotype	Condition	Treatment	Duration (wks)
1	Treatment-naïve with or without cirrhosis	Harvoni	12*
1	Treatment-experienced** without cirrhosis	Harvoni	12
1	Treatment-experienced** with cirrhosis	Harvoni	24

*HARVONI for 8 weeks can be considered in treatment-naïve patients without cirrhosis who have pretreatment HCV RNA less than 6 million IU/mL *[see Clinical Studies (14)]*.

**Treatment-experienced patients who have failed treatment with either peginterferon alfa + ribavirin or an HCV protease inhibitor + peginterferon alfa + ribavirin.

Table 5: FDA Approved HCV Treatment Ombitasvir / Paritaprevir / Ritonavir with Dasabuvir (VIEKIRA PAK)

Genotype	Condition	Treatment*	Duration (wks)
1a*	Without cirrhosis	VIEKIRA PAK + ribavirin	12
1a	With cirrhosis	VIEKIRA PAK + ribavirin	24**
1b	Without cirrhosis	VIEKIRA PAK	12
1b	With cirrhosis	VIEKIRA PAK + ribavirin	12

*Note: Follow the genotype 1a dosing recommendations in patients with an unknown genotype 1 subtype or with mixed genotype 1 infection.

**VIEKIRA PAK administered with ribavirin for 12 weeks may be considered for some patients based on prior treatment history [see Clinical Studies (14.3)].

Table 6: FDA Approved HCV Treatment with Simeprevir / Sofosbuvir Combination

Genotype	Condition	Treatment*	Duration (wks)
1	Treatment-naïve and treatment-experienced* without cirrhosis	simeprevir + sofosbuvir	12
1	Treatment-naïve and treatment-experienced* with cirrhosis	simeprevir + sofosbuvir	24

*Treatment-experienced patients include prior relapsers, prior partial responders and prior null responders who failed prior IFN-based therapy.

Appendix B: Chronic Hepatitis C Virus Infection and Liver Transplantation

Patients with decompensated liver disease or hepatocellular carcinoma (HCC) who are considered candidates for liver transplantation will need to be evaluated by liver transplant surgeon. If the transplant surgeon recommends the treatment of chronic Hepatitis C virus infection (HCV) as part of the preparation to be cleared for transplant, the treatment of chronic HCV can be considered medically necessary and covered by the Medicaid health plan.

In patients with HCC, the Milan criteria is used as a general guide to determine HCC candidates for liver transplantation. In addition, on a rare exception, the transplant surgeon can also make a recommendation for liver transplantation for a patient that may not meet Milan criteria.

Milan Criteria

The Milan criteria are a generally accepted set of criteria to assess suitability in patients with cirrhosis and hepatocellular carcinoma for liver transplantation.

According to the Milan criteria, in order to be suitable for a liver transplantation one needs to have:

- No lesion larger than 5 cm
- ≤ 3 lesions with diameter ≤ 3 cm
- No extrahepatic involvement
- No major vessel involvement

Appendix C: Child-Pugh Score

The Child-Pugh Score, also known as Child-Turcotte-Pugh (CTP) score, is a scoring system for severity of liver disease and likelihood of survival based on the presence of degenerative disease of the brain (encephalopathy), the escape or accumulation of fluid in the abdominal cavity (ascites), laboratory measures of various substances in the blood (see table below), and the presence of other co-existing diseases; after calculating the CTP score using a table similar to the one below, individuals can be classified into one of three categories:

- Childs A (5-6 points): 10 year survival 80-90%,
- Childs B (7-9 points): 5 year survival 60-80%, and
- Childs C (10-15 points): 2 year survival less than 50%.

Table 7: Child-Pugh Score

Variable	1 Point	2 Points	3 Points
Encephalopathy	None	Moderate	Severe
Ascites	None	Mild	Moderate
Albumin (mg/dL)	Greater than 3.5	2.8 – 3.5	Less than 2.8
Prothrombin time (International Normalized ratio) prolonged	Less than 4	4 – 6	Greater than 6
Bilirubin (mg/dL) Primary biliary cirrhosis Cirrhosis/primary Primary sclerosing cholangitis	1 - 4	4 – 10	Greater than 10
All other diseases	Less than 2	1 – 3	Greater than 3

Compensated liver disease: Child-Pugh score less than or equal to 6 (class A) in cirrhotic individuals before or during treatment.

Decompensated liver disease: Child-Pugh score greater than 6 (class B or class C) in cirrhotic individuals before or during treatment.

Appendix D: Contraindications for Chronic Hepatitis C Virus Infection Treatment

Table 8: FDA Absolute Contraindications for DAA and Related Medications

	Peg-IF (IFN)	Ribavirin (RBV)	Olysio + Sovaldi	Sovaldi	Sovaldi + IFN + RBV	Harvoni	Viekira
Hypersensitivity	X	X			X (IFN or RBV)		X (ritonavir or RBV)
Autoimmune hepatitis	X				X		
Decompensated liver disease	X		X	*	X	*	X
Pregnant women or men whose female partners are pregnant		X		X w/RBV	X w/RBV		X w/RBV
Co-administration of didanosine		X		X w/RBV	X		X w/RBV
Hemoglobinopathies		X		X w/RBV	X		X w/RBV
Use of CYP3A, CYP2C8 and strong inhibitors of CYP2C8							X

*Safety and efficacy of SOVALDI have not been established in patients with decompensated cirrhosis.

Absolute Contraindications as per prescribing information for peg-interferon, ribavirin, simeprevir (Olysio), sofosbuvir (Sovaldi), ledipasvir and sofosbuvir (Harvoni) and ombitasvir, paritaprevir and ritonavir plus dasabuvir (Viekira Pak), accessed April 2015.

Ribavirin CONTRAINDICATIONS

FDA approved treatment regimens for SOVALDI and VIEKIRA can include ribavirin. SOVALDI combination treatment with ribavirin or peginterferon alfa/ribavirin and VIEKIRA combination with ribavirin are contraindicated in women who are pregnant and men whose female partners are pregnant because of the risks for birth defects and fetal death associated with ribavirin.

Ribavirin and Pregnancy Warnings: Pregnancy Category X

Ribavirin may cause birth defects and/or death of the exposed fetus and animal studies have shown that interferons have abortifacient effects. Extreme care must be taken to avoid pregnancy in female patients and in female partners of male patients. Ribavirin therapy should not be started unless a report of a negative pregnancy test has been obtained immediately prior to initiation of therapy.

Women of childbearing potential and their male partners must not receive ribavirin unless use two forms of effective contraception during treatment and for at least 6 months after treatment has concluded. Routine monthly pregnancy tests must be performed during this time. Two non-hormonal methods of contraception should be used during treatment with SOVALDI or VIEKIRA and concomitant ribavirin.

In case of exposure during pregnancy, a Ribavirin Pregnancy Registry has been established to monitor maternal-fetal outcomes of pregnancies in female patients and female partners of male patients exposed to ribavirin during treatment and for 6 months following cessation of treatment. Healthcare providers and patients are encouraged to report such cases by calling Ribavirin Pregnancy Registry at 1-800-593-2214. For patients who are HCV/HIV-1 co-infected and taking concomitant antiretrovirals, an Antiretroviral Pregnancy Registry is also available at 1-800-258-4263.

The treatment of HCV infection is rapidly changing with 7 new DAA medications receiving FDA approval within the past 4 years. The first generation DAA's, boceprevir and telaprevir, FDA approved in 2011, and the second generation, simeprevir, FDA approved in 2013, have since been replaced with newer DAA's and DAA combination treatment regimens.

Health plans must continually update policies for new FDA approved therapies and monitor for FDA warnings in the rapidly changing field of DAA therapies. This memorandum serves as broad guidance for the treatment of Hepatitis C. Health plans must also monitor warnings and contraindications for each DAA medication including drug-drug interactions and warnings regarding supplement use.

References:

1) American Association for The Study of Liver Disease Treatment (AASLD): Recommendations for Testing, Managing, and Treating Hepatitis C, updated on April 8, 2015. www.hcvguidelines.org/full-report-view
2) Afdhal N, Reddy R, Nelson D, Lawitz E, Gordon S, Schiff E, et al. Ledipasvir and Sofosbuvir for previously treated HCV Genotype 1 Infection (ION2). N Engl J Med 2014; 370: 1483-93
3) Afdhal N, Zeuzem S, Kwo P, Chojkier M, Gitlin N, Puoti M, et al. Ledipasvir and Sofosbuvir for Untreated HCV Genotype 1 infection (ION1). N Engl J Med 2014;370:1889-98
4) Department of Veterans Affairs National Hepatitis C Resource Center Program and the Office of Public Health (VA): Chronic Hepatitis C Virus Infection: Treatment Considerations, updated February 17, 2015. www.hepatitis.va.gov/provider/guidelines/2014hcv/index.asp
5) Food and Drug Administration. www.FDA.gov
6) Kowdley K, Gordon S, Reddy R, Rossaro L, Bernstein D, Lawitz E, et al. Ledipasvir and Sofosbuvir for 8 or 12 Weeks for Chronic HCV without Cirrhosis (ION3). N Engl J Med 2014; 370: 1879-88