I. Description

The diagnosis of chronic hepatitis C virus (HCV) infection is based on the presence of both anti-HCV antibodies, detected by enzyme immunoassays, and HCV RNA, detected by molecular amplification (polymerase chain reaction). HCV RNA can be detected in blood within one to three weeks after exposure, and anti-HCV seroconversion occurs by eight to nine weeks after exposure.

Progression of chronic hepatitis C infection to end stage liver disease most commonly occurs over several decades. Early in the course of infection, serum or liver-related enzyme levels, such as alanine aminotransferase, aspartate aminotransferase, and γ-glutamyltranspeptidase may be elevated but there are no signs of liver dysfunction. As the disease progresses, signs of liver fibrosis may develop and fibrosis will often progress to cirrhosis. However, many patients may go decades or a lifetime without substantial liver damage. Early damage to the liver (including fibrosis) is generally reversible, while cirrhosis may not be reversible. Disease progression is accelerated in the presence of co-factors such as alcohol consumption, diabetes mellitus, older age at acquisition, HIV co-infection, and co-infection with other hepatic viruses.

Direct acting antiviral (DAA) medications for hepatitis C specifically target proteins involved in the HCV life cycle and disrupt viral replication. In patients with chronic hepatitis C, these medications offer the potential to improve cure rates with lower toxicity compared to treatment regimens that do not include DAAs.
Direct Acting Antiviral Medications for Treatment of Hepatitis C

HMO/PPO Formulary Effective as of 1-1-18

<table>
<thead>
<tr>
<th>Preferred formulary options</th>
<th>Harvoni</th>
<th>Epclusa</th>
<th>Mavyret</th>
<th>Vosevi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Preferred Non-Formulary</td>
<td>Daklinza</td>
<td>Olysio</td>
<td>Sovaldi</td>
<td>Technivie</td>
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</tbody>
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The combined American Association for the Study of Liver Diseases (AASLD) and Infectious Diseases Society of America (IDSA) guidelines for the treatment of chronic hepatitis C are available at http://www.hcvguidelines.org/. These guidelines are updated frequently, so providers should check them periodically for the most up to date recommendations on patient care. The recommendations in these guidelines are a valuable resource for this policy but do not alone form a basis for approval of a particular course of treatment.

II. General Criteria/Guidelines

A. DAA medications are covered for the treatment of HCV infection (subject to Limitations and Administrative Guidelines) when all of the following criteria are met:
   1. Patient is of approved age as indicated by current FDA approvals
   2. The prescribing physician attests that the patient is at low risk for noncompliance with the treatment regimen
   3. The patient has an HCV RNA positive diagnosis documented by a quantitative titer
   4. The patient has no history of alcohol or substance abuse within the three months prior to treatment initiation
   5. The medication is being prescribed by, or in consultation with, one of the following specialists:
      a. Hepatologist;
      b. Gastroenterologist;
      c. Infectious Disease Specialist; or
      d. HIV Specialist
   6. The patient agrees to the following:
      a. 100% medication compliance;
      b. Regular follow-up with specialty pharmacist or treating provider;
      c. No alcohol or illicit drug use during the course of treatment;
      d. Drug testing, when recommended by the treating provider; and
e. Blood draws to measure HCV RNA, when ordered.

7. Treatment is in accordance with FDA approved treatment regimens unless otherwise noted in drug-specific criteria/guidelines (refer to Drug-Specific Criteria/Guidelines)

B. Patients who experienced prior treatment failure may be treated as outlined in the drug-specific criteria/guidelines within Criteria for Approval section for specific genotype (refer to Drug-Specific Criteria/Guidelines).

III. Formulary/Preferred Drug Requirements

A. For HMO/PPO members, the following DAA’s are preferred options: Harvoni, Epclusa, Mavyret, Vosevi. Requests for non-formulary/non-preferred DAAs will be considered in the following situations:
   1. Member had an inadequate treatment response with a formulary/preferred option (see IV.D. below)
   2. Member has a contraindication to a formulary/preferred option
   3. Member has a history of intolerance or an adverse event due to previous treatment with a formulary/preferred option

B. Formulary/preferred drug exceptions criteria are not required for members who are continuing a course of treatment with the requested non-formulary/non-preferred DAA medication.

IV. Limitations

A. Treatment of HCV with DAA medication is not covered when any of the general criteria and formulary/preferred drug requirements specified above (Sections II and III) are not met.

B. Treatment of HCV with DAA medication is not covered for patients with a life expectancy estimated to be less than 12 months, due to comorbid conditions.

C. Treatment is contraindicated in patients with a known hypersensitivity or allergy to the prescribed drug used to treat hepatitis C.

D. Repeat treatments in any of the following situations will not be covered:
   1. Inadequate compliance resulting in failure to achieve sustained viral response (SVR);
   2. Reinfection; or
   3. Discontinuation of treatment secondary to harmful alcohol and/or drug abuse

E. The plan will not cover replacement medication for pills that are lost or stolen.

V. Dosage and Administration

A. Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

B. A 28-day supply dispense limit applies to all targeted hepatitis C agents in order to better manage the therapy regimen.

VI. Administrative Guidelines
Prior authorization is required. To preauthorize Hep C therapy, contact CVS Specialty Guideline Management (SGM) at (808) 254-4414.

A. The following medical record documentation, as applicable to the patient, must be submitted with the prior authorization request:
   1. Written treatment plan from the requesting provider
   2. Documentation that the member has been assessed for potential non-adherence to treatment regimen
   3. HCV RNA laboratory report with viral load and genotype
   4. Laboratory testing for resistance associated variants (RAVs) (refer to drug-specific criteria for details)
      a. Harvoni and Epclusa: NS5A inhibitor RAVs where applicable
      b. Olysio: NS3 Q80K polymorphism, NS5A inhibitor RAVs, or NS3 protease inhibitor RAVs where applicable
      c. Zepatier for genotype 1a: baseline NS5A polymorphisms

B. A specialty pharmacy will dispense no more than 28 days of medication at one time.

C. The HMSA Hepatitis C Treatment Checklist can be found in Appendix A. This checklist, completed and signed by the patient, is required prior to initiation of treatment.

D. This policy is not applicable to Medicare Advantage members.

VII. Appendix
### Appendix A

**HMSA Hepatitis C Treatment Checklist**

**HMSA HEPATITIS C TREATMENT CHECKLIST**

Coverage of Direct Acting Antiviral medications for the treatment of Hepatitis C is covered only if you meet HMSA policies and guidelines related to the treatment. You must comply with all instructions given to you by your physician and pharmacy, and agree to avoid all activities that may worsen your liver disease or infect yourself or others with the hepatitis C virus or other bloodborne pathogens. By initialing 1 through 8 and signing below where indicated you promise to comply with the requirements of this checklist.

Please initial in the space provided next to each statement below. By initialing you agree to comply with each statement.

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>I agree to comply with all instructions from my physician and dispensing pharmacy related to the medication prescribed and dispensed to me.</td>
</tr>
<tr>
<td>2.</td>
<td>I agree to keep all appointments scheduled with my physician.</td>
</tr>
<tr>
<td>3.</td>
<td>I agree to not use alcohol or illicit drugs for the 3 months preceding and during treatment for hepatitis C.</td>
</tr>
<tr>
<td>4.</td>
<td>I agree to attend Alcoholics Anonymous (AA), Narcotics Anonymous (NA) or a similar program for substance abuse, if recommended by my physician.</td>
</tr>
<tr>
<td>5.</td>
<td>I agree to use only the medications prescribed by my physician.</td>
</tr>
<tr>
<td>6.</td>
<td>I agree to random drug and alcohol testing, if requested by my physician.</td>
</tr>
<tr>
<td>7.</td>
<td>I agree to routine blood testing for the hepatitis C virus when ordered by my physician.</td>
</tr>
<tr>
<td>8.</td>
<td>I understand that this treatment for hepatitis C is intended to be a once per lifetime treatment.</td>
</tr>
</tbody>
</table>

By signing below I am indicating that I will comply with 1 through 8 above. I have had an opportunity to ask questions about this form and my questions have been answered to my satisfaction. I understand that payment by HMSA of the medication prescribed by my physician to treat hepatitis C is dependent upon my compliance with the statements above. I further understand that HMSA will discontinue payment for treatment with my medication to treat hepatitis C if at any time I am not compliant with 1 through 8 above. I further understand that HMSA will not pay to replace the medication prescribed if the medication is lost, stolen, destroyed or otherwise not available to me.

**Patient Name:** __________________________

**Patient Signature:** _______________________

**Date:** __________________________
VIII. Drug-Specific Criteria/Guideline
Drug specific criteria begin on page 6.

HARVONI
(ledipasvir and sofosbuvir)

I. INDICATIONS

FDA-Approved Indications
Harvoni is indicated with or without ribavirin for the treatment of patients with chronic hepatitis C virus (HCV) genotype 1, 4, 5 or 6 infection.

II. EXCLUSIONS
When the requested drug is being used in a combination therapy regimen, exclusions to the other antiviral drugs also apply.

III. CRITERIA FOR APPROVAL
1. Chronic hepatitis C virus infection, without ribavirin
   1.1 Genotype 1 infection
      a. Authorization of up to 12 weeks total may be granted for treatment-naïve members with compensated cirrhosis.
      b. Authorization of up to 8 weeks total may be granted for treatment-naïve members without cirrhosis who have pre-treatment HCV RNA below 6 million IU/mL and are HIV-uninfected and non-African American.
      c. Authorization of up to 12 weeks total may be granted for treatment-naïve members without cirrhosis who have pre-treatment HCV RNA greater than or equal to 6 million IU/mL, HIV co-infection, are African American, or are less than 18 years of age.
      d. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with peginterferon alfa (PEG-IFN) and ribavirin (RBV) with or without an HCV protease inhibitor (telaprevir, boceprevir, or simeprevir).
      e. Authorization of up to 24 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor.

   1.2 Genotype 4 infection
      a. Authorization of up to 12 weeks total may be granted for treatment-naïve members without cirrhosis or with compensated cirrhosis.
      b. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor.
1.3 Genotype 5 infection
Authorization of up to 12 weeks total may be granted for members who are treatment-naïve or who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor.

1.4 Genotype 6 infection
Authorization of up to 12 weeks total may be granted for members who are treatment-naïve or who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor.

1.5 Decompensated cirrhosis (CTP class B or C)
Authorization of up to 24 weeks total may be granted for members with HCV genotype 1, 4, 5 or 6 infection and documented anemia (baseline Hgb below 10 g/dL) or RBV ineligibility (see Section IV).

1.6 Kidney transplant recipients
Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have HCV genotype 1 or 4 infection.

2. Chronic hepatitis C virus infection, in combination with ribavirin
2.1 Genotype 1 infection
a. Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor.
b. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with sofosbuvir plus RBV with or without PEG-IFN.

2.2 Genotype 4 infection
Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor.

2.3 Decompensated cirrhosis (CTP class B or C)
a. Authorization of up to 12 weeks total may be granted for members with HCV genotype 1, 4, 5 or 6 infection.
b. Authorization of up to 24 weeks total may be granted for members with HCV genotype 1, 4, 5 or 6 infection who failed prior treatment with a sofosbuvir-based regimen (eg, sofosbuvir and RBV, sofosbuvir plus PEG-IFN and RBV, sofosbuvir plus simeprevir with or without RBV).
c. Authorization of up to 12 weeks total may be granted for members with recurrent HCV genotype 1, 4, 5 or 6 infection post liver transplantation and decompensated cirrhosis (see section 2.4 below).
2.4 Recurrent HCV infection post liver transplantation
Authorization of up to 12 weeks total may be granted for members with recurrent HCV genotype 1, 4, 5 or 6 infection post liver transplantation.

3. HCV and HIV coinfection
Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section III above are met.

IV. APPENDIX
RIBAVIRIN INELIGIBILITY
RBV ineligibility is defined as one or more of the below:
A. Intolerance to RBV
B. Pregnant female or male whose female partner is pregnant
C. Hemoglobinopathy
D. Coadministration with didanosine
E. History or significant or unstable cardiac disease
**VIEKIRA PAK**  
**VIEKIRA XR**  
*(ombitasvir/paritaprevir/ritonavir with dasabuvir)*

I. **INDICATIONS**

FDA-Approved Indications  
Viekira Pak/Viekira XR with or without ribavirin is indicated for the treatment of adult patients with genotype 1 chronic hepatitis C virus (HCV) infection including those with compensated cirrhosis.

II. **EXCLUSIONS**

Decompensated cirrhosis/moderate or severe hepatic impairment (Child Turcotte Pugh Class B or C)

Note: When the requested drug is being used in a combination therapy regimen, exclusions to the other antiviral drugs also apply.

III. **CRITERIA FOR APPROVAL**

1. **Chronic hepatitis C virus infection, in combination with ribavirin (RBV)**  
   Note: Members with mixed genotype 1 infection or unknown genotype 1 subtype should follow the criteria for approval for genotype 1a infection.

   1.1 **Genotype 1a infection**
   a. Authorization of up to 12 weeks total may be granted for members without cirrhosis who meet one of the following criteria:
      i. Treatment-naïve
      ii. Failed prior treatment with peginterferon alfa (PEG-IFN) and RBV.
   b. Authorization of up to 24 weeks total may be granted for members with compensated cirrhosis who meet one of the following criteria:
      i. Treatment-naïve
      ii. Failed prior treatment with PEG-IFN and RBV.

   1.2 **Recurrent HCV infection post liver transplantation**
   Authorization of up to 24 weeks total may be granted for members with recurrent HCV infection post liver transplantation who meet all of the following criteria:
   a. Genotype 1 infection (irrespective of subtype)
   b. Metavir fibrosis score of 2 or lower

2. **Chronic hepatitis C virus infection, without RBV**  

   **Genotype 1b infection**
   Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who meet one of the following criteria:
   a. Treatment-naïve
   b. Failed prior treatment with PEG-IFN and RBV
3. **HCV and HIV coinfection**
   Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in section III above are met.
SOVALDI (sofosbuvir)

I. INDICATIONS

FDA-Approved Indications
1. Sovaldi is indicated for the treatment of adult patients with genotype 1, 2, 3 or 4 chronic hepatitis C virus (HCV) infection as a component of a combination antiviral treatment regimen.
2. Sovaldi is indicated for the treatment of pediatric patients 12 years of age and older or weighing at least 35 kg with genotype 2 or 3 chronic HCV infection.

Compendial Uses
Chronic hepatitis C genotype 5 or 6 infection

II. EXCLUSIONS
When the requested drug is being used in a combination therapy regimen, exclusions to the other antiviral drugs also apply.

III. CRITERIA FOR APPROVAL
1. Chronic hepatitis C virus infection, in combination with peginterferon alfa (PEG-IFN) and ribavirin (RBV)
   1.1 Genotype 1 infection
      Authorization of up to 12 weeks total may be granted for members who are treatment-naïve or who failed prior treatment with PEG-IFN and RBV.
   1.2 Genotype 4 infection
      Authorization of up to 12 weeks total may be granted for members who are treatment-naïve or who failed prior treatment with PEG-IFN and RBV.

2. Chronic hepatitis C virus infection, in combination with RBV
   2.1 Genotype 1 infection
      Authorization of up to 24 weeks total may be granted for members who have documented interferon (IFN) ineligibility (see Section IV).
   2.2 Genotype 2 infection
      Authorization of up to 12 weeks total may be granted for members who are treatment-naïve or failed prior treatment with PEG-IFN and RBV.
   2.3 Genotype 3 infection
      Authorization of up to 24 weeks total may be granted for members who are treatment-naïve or failed prior treatment with PEG-IFN and RBV.
   2.4 Members with hepatocellular carcinoma awaiting liver transplantation
      Authorization of up to 48 weeks total or until liver transplantation, whichever occurs first, may be granted for members with genotype 1, 2, 3, or 4 infection and hepatocellular carcinoma who meet the MILAN criteria, defined as the following:
      a. Tumor size 5 cm or less in diameter with single hepatocellular carcinomas OR 3 tumor nodules or less, each 3 cm or less in diameter with multiple tumors AND
      b. No extrahepatic manifestations of the cancer or evidence of vascular invasion of tumor
3. **Chronic hepatitis C virus infection, in combination with Olysio (with or without RBV)**

   Authorization of up to 24 weeks total (as applicable) may be granted for members prescribed Sovaldi in combination with Olysio (with or without ribavirin as applicable) who meet the criteria for approval for the requested regimen. Refer to the Olysio section of this policy for the specific criteria for approval and approval durations.

4. **Chronic hepatitis C virus infection, in combination with Daklinza (with or without ribavirin)**

   Authorization of up to 24 weeks total (as applicable) may be granted for members prescribed Sovaldi in combination with Daklinza (with or without ribavirin as applicable) who meet the criteria for approval for the requested regimen. Refer to the Daklinza section of this policy for the specific criteria for approval and approval durations.

5. **Chronic hepatitis C virus infection, in combination with Zepatier**

   Authorization of up to 12 weeks total (as applicable) may be granted for members prescribed Sovaldi in combination with Zepatier who meet the criteria for approval for the requested regimen. Refer to the Zepatier section of this policy for the specific criteria for approval and approval durations.

6. **HCV and HIV coinfection**

   Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in section III above are met.

### IV. APPENDIX

**INTERFERON INELIGIBILITY**

IFN ineligible is defined as one or more of the below:

- A. Intolerance to IFN
- B. Autoimmune hepatitis and other autoimmune disorders
- C. Hypersensitivity to PEG-IFN or any of its components
- D. Major uncontrolled depressive illness
- E. A baseline neutrophil count < 1,500/mcL
- F. A baseline platelet count < 90,000/mcL
- G. A baseline hemoglobin < 10 g/dL
- H. History of pre-existing cardiac disease
DAKLINZA (daclatasvir)

I. INDICATIONS

FDA-Approved Indication
Daklinza is indicated for use with sofosbuvir, with or without ribavirin, for the treatment of patients with chronic hepatitis C virus (HCV) genotype 1 or 3 infection.

Limitations of Use:
Sustained virologic response (SVR) rates are reduced in HCV genotype 3-infected patients with cirrhosis receiving Daklinza in combination with sofosbuvir for 12 weeks.

Compendial Uses
Chronic hepatitis C genotype 2, 4, 5 or 6 infection

II. EXCLUSIONS
When the requested drug is being used in a combination therapy regimen, exclusions to the other antiviral drugs also apply.

III. CRITERIA FOR APPROVAL

1. Chronic hepatitis C virus infection, in combination with Sovaldi
   1.1 Genotype 1 infection
      a. Authorization of up to 12 weeks total may be granted for treatment-naive members without cirrhosis or with compensated cirrhosis.
      b. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with PEG-IFN and RBV.

   1.2 Genotype 2 infection
      a. Authorization of up to 12 weeks total may be granted for treatment-naive members without cirrhosis.
      b. Authorization of up to 24 weeks total may be granted for treatment-naive members with compensated cirrhosis.
      c. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with PEG-IFN and RBV.
      d. Authorization of up to 24 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV.

   1.3 Genotype 3 infection
      a. Authorization of up to 12 weeks total may be granted for treatment-naive members without cirrhosis.
      b. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with peginterferon alfa (PEG-IFN) and ribavirin (RBV).
      c. Authorization of up to 24 weeks total may be granted for treatment-naive members with compensated cirrhosis.
1.4 Decompensated cirrhosis (Child Turcotte Pugh [CTP] class B or C)
Authorization of up to 24 weeks total may be granted for members with HCV genotype 1, 2, 3 or 4 infection and documented anemia (baseline hemoglobin [Hgb] below 10 g/dL) or RBV ineligibility (see Section IV).

2. Chronic hepatitis C virus, in combination with Sovaldi and RBV
2.1 Genotype 3 infection
a. Authorization of up to 24 weeks total may be granted for treatment-naive members with compensated cirrhosis.
b. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with PEG-IFN and RBV and have the Y93H substitution associated with daclatasvir resistance.

2.2 Decompensated cirrhosis (CTP class B or C)
Authorization of up to 12 weeks total may be granted for members with HCV genotype 1, 2, 3 or 4 infection.

2.3 Recurrent HCV infection post liver transplantation
a. Authorization of up to 12 weeks total may be granted for members with recurrent HCV genotype 1, 2, or 3 infection post liver transplantation.
b. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have recurrent HCV genotype 4, 5, or 6 infection post liver transplantation.

2.4 Kidney transplant recipients
Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have HCV genotype 2, 3, 5 or 6 infection.

3. HCV and HIV coinfection
Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in section III above are met.

4. APPENDIX
RIBAVIRIN INELIGIBILITY
RBV ineligibility is defined as one or more of the below:
A. Intolerance to RBV
B. Pregnant female or male whose female partner is pregnant
C. Hemoglobinopathy
D. Coadministration with didanosine
E. History of significant or unstable cardiac disease
TECHNIVIE
(ombitasvir/paritaprevir/ritonavir)

I. INDICATIONS

FDA-Approved Indications
Technivie is indicated in combination with ribavirin for the treatment of patients with genotype 4 chronic hepatitis C virus (HCV) infection without cirrhosis or with compensated cirrhosis.

II. EXCLUSIONS
Decompensated cirrhosis/moderate or severe hepatic impairment (Child Turcotte Pugh Class B or C)

Note: When the requested drug is being used in a combination therapy regimen, exclusions to the other antiviral drugs also apply.

III. CRITERIA FOR APPROVAL
1. Chronic hepatitis C virus infection, in combination with ribavirin (RBV)
   Genotype 4 infection
   Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who meet one of the following criteria:
   i. Treatment-naive
   ii. Failed prior treatment with peginterferon alfa and RBV

2. Chronic hepatitis C virus infection, without RBV
   Genotype 4 infection
   Authorization of up to 12 weeks total may be granted for members without cirrhosis who meet all of the following criteria:
   i. Treatment-naive
   ii. Member has intolerance to RBV, has documented anemia (baseline hemoglobin below 10 g/dL) or RBV ineligibility (see Section V for ribavirin ineligibility)

3. HCV and HIV coinfection
   Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section III above are met.

IV. APPENDIX: RIBAVIRIN INELIGIBILITY
RBV ineligibility is defined as one or more of the below:
A. Pregnant female or male whose female partner is pregnant
B. Hemoglobinopathy
C. Coadministration with didanosine
D. History of significant or unstable cardiac disease
ZEPATIER (elbasvir and grazoprevir)

I. INDICATIONS

FDA-Approved Indications
Zepatier is indicated for the treatment of chronic hepatitis C virus genotypes 1 or 4 infection in adults. Zepatier is indicated for use with ribavirin in certain patient populations.

Compendial Uses
Chronic hepatitis C genotype 3 infection

II. EXCLUSIONS
Decompensated cirrhosis/moderate or severe hepatic impairment (Child Turcotte Pugh Class B or C)

Note: When the requested drug is being used in a combination therapy regimen, exclusions to the other antiviral drugs also apply.

III. CRITERIA FOR APPROVAL

1. Chronic hepatitis C virus infection, in combination with ribavirin (RBV)
   1.1 Genotype 1a infection
      a. Authorization of up to 16 weeks total may be granted for members with baseline NS5A resistance-associated substitutions (RASs)/polymorphisms (see Section V) who are either of the following:
         i. Treatment-naïve
         ii. Failed prior treatment with peginterferon alfa (PEG-IFN) and RBV with or without an HCV protease inhibitor (boceprevir, simeprevir or telaprevir)
      b. Authorization of up to 12 weeks total may be granted for members without baseline NS5A resistance-associated substitutions (RASs)/polymorphisms (see Section V) who have failed prior treatment with PEG-IFN and RBV with an HCV protease inhibitor (boceprevir, simeprevir or telaprevir).

   1.2 Genotype 1b infection
      Authorization of up to 12 weeks total may be granted for members who failed prior treatment with PEG-IFN and RBV with an HCV protease inhibitor (boceprevir, simeprevir or telaprevir).

   1.3 Genotype 4 infection
      Authorization of up to 16 weeks total may be granted for members who failed prior treatment with PEG-IFN and RBV.

2. Chronic hepatitis C virus infection, without RBV
2.1 Genotype 1a infection
   a. Authorization of up to 12 weeks total may be granted for members with end-stage renal disease (ESRD) or severe renal impairment (estimated glomerular filtration rate [eGFR] of less than 30 mL/min/1.73m²).
   b. Authorization of up to 12 weeks total may be granted for members without baseline NS5A resistance-associated substitutions (RASs)/polymorphisms who are either of the following:
      i. Treatment-naïve
      ii. Failed prior treatment with PEG-IFN and RBV without an HCV protease inhibitor (boceprevir, simeprevir or telaprevir)

2.2 Genotype 1b infection
   Authorization of up to 12 weeks total may be granted for members who are either of the following:
   a. Treatment-naïve
   b. Failed prior treatment with PEG-IFN and RBV without an HCV protease inhibitor (boceprevir, simeprevir or telaprevir)

2.3 Genotype 4 infection
   Authorization of up to 12 weeks total may be granted for members who are either of the following:
   a. Treatment-naïve
   b. Failed prior treatment with PEG-IFN and RBV

3. Chronic hepatitis C virus infection, in combination with Sovaldi
   Genotype 3 infection
   Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV.

4. HCV and HIV coinfection
   Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section III above are met.

IV. APPENDIX: NS5A RESISTANCE-ASSOCIATED SUBSTITUTIONS (POLYMORPHISMS)
NS5A resistance-associated substitutions (polymorphisms) at amino acid positions M28, Q30, L31 or Y93. Examples include M28A/T, Q30H/R, L31M/V, and Y93C/H/N.
EPCLUSA (sofosbuvir and velpatasvir)

I. INDICATIONS

FDA-Approved Indications
Epclusa is indicated for the treatment of adult patients with chronic hepatitis C virus (HCV) genotype 1, 2, 3, 4, 5 or 6 infection:
A. without cirrhosis or with compensated cirrhosis
B. with decompensated cirrhosis for use in combination with ribavirin

II. CRITERIA FOR APPROVAL

1. Chronic hepatitis C virus infection (without ribavirin)

1.1 Genotype 1 infection
a. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naive or who failed prior treatment with peginterferon alfa (PEG-IFN) and ribavirin (RBV) with or without an HCV protease inhibitor (boceprevir, simeprevir or telaprevir).

1.2 Genotype 2 infection
a. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naive or who failed prior treatment with PEG-IFN and ribavirin.

1.3 Genotype 3 infection
Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naive or who failed prior treatment with PEG-IFN and RBV.

1.4 Genotype 4, 5 or 6 infection
Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naive or who failed prior treatment with PEG-IFN and ribavirin with or without an HCV protease inhibitor (boceprevir, simeprevir or telaprevir).

1.5 Decompensated cirrhosis (Child Turcotte Pugh [CTP] class B or C)
Authorization of up to 24 weeks total may be granted for members with genotype 1, 2, 3,
4, 5 or 6 infection who have decompensated cirrhosis and documented anemia (baseline hemoglobin [Hgb] below 10 g/dL) or RBV ineligibility (see Section III).

2. **Chronic hepatitis C virus infection, in combination with ribavirin**
   
   2.1 **Genotype 3 infection**
   
   a. Authorization of up to 12 weeks total may be granted for members with the Y93H substitution associated with velpatasvir resistance who are either of the following:
      
      i. Treatment-naïve with compensated cirrhosis
      
      ii. Failed prior treatment with PEG-IFN and ribavirin without cirrhosis
   
   b. Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and ribavirin.

   2.2 ** Decompensated cirrhosis (CTP class B or C)**
   
   a. Authorization of up to 12 weeks total may be granted for members with genotype 1, 2, 3, 4, 5 or 6 infection and decompensated cirrhosis.
   
   b. Authorization of up to 24 weeks total may be granted for members with genotype 1, 2, 3, 4, 5 or 6 infection and decompensated cirrhosis who failed prior treatment with a sofosbuvir- or NS5A inhibitor-based regimen.

   2.3 **Recurrent HCV infection post liver transplantation**
   
   Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis or decompensated cirrhosis and recurrent HCV genotype 2 or 3 infection post liver transplantation.

3. **HCV and HIV coinfection**
   
   Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section II above are met.

III. **APPENDIX**

**RIBAVIRIN INELIGIBILITY**

RBV ineligibility is defined as one or more of the below:

A. Intolerance to RBV
B. Pregnant female or male whose female partner is pregnant
C. Hemoglobinopathy
D. Coadministration with didanosine
E. History of significant or unstable cardiac disease
OLYSIO (simeprevir)

I. INDICATIONS

FDA-Approved Indications
Olysio is a hepatitis C virus (HCV) NS3/4A protease inhibitor indicated for the treatment of adults with chronic hepatitis C genotype 1 or 4 infection as a component of a combination antiviral treatment regimen.

II. EXCLUSIONS
Decompensated cirrhosis/moderate or severe hepatic impairment (Child Turcotte Pugh Class B or C)

Note: When the requested drug is being used in a combination therapy regimen, exclusions to the other antiviral drugs also apply.

III. CRITERIA FOR APPROVAL

1. Chronic hepatitis C virus infection, in combination with PEG-IFN and RBV
   Genotype 1 or 4 infection
   Authorization of up to 6 weeks total may be granted for initiation of therapy in members who are treatment-naïve or failed prior treatment with PEG-IFN and RBV AND meet one of the following criteria:
   A. Genotype 1a infection without the NS3 Q80K polymorphism
   B. Genotype 1b infection
   C. Genotype 4 infection

2. Chronic hepatitis C virus infection, in combination with Sovaldi
   2.1 Genotype 1a infection
   A. Authorization of up to 12 weeks total may be granted for members without cirrhosis who are treatment-naïve or failed prior treatment with PEG-IFN and RBV.
   B. Authorization of up to 24 weeks total may be granted for members with compensated cirrhosis without the NS3 Q80K polymorphism who are treatment-naïve or failed prior treatment with PEG-IFN and RBV.
   2.2 Genotype 1b infection
   A. Authorization of up to 12 weeks total may be granted for members without cirrhosis who are treatment-naïve or failed prior treatment with PEG-IFN and RBV.
   B. Authorization of up to 24 weeks total may be granted for members with compensated cirrhosis who are treatment-naïve or failed prior treatment with PEG-IFN and RBV.
2.3 Recurrent HCV infection post liver transplantation
Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have recurrent HCV genotype 1 or 4 infection post liver transplantation.

3. Chronic hepatitis C virus infection, in combination with Sovaldi and RBV
Recurrent HCV infection post liver transplantation
Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have recurrent HCV genotype 1 or 4 infection post liver transplantation.

4. HCV and HIV Coinfection
Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in section III above are met.

IV. CONTINUATION OF THERAPY
Chronic hepatitis C virus infection, in combination with PEG-IFN and RBV
Genotype 1 or 4 infection at week 4 assessment
Authorization of up to 12 weeks total for Olysio and up to 48 weeks total for PEG-IFN and RBV may be granted for members with HCV-RNA < 25 IU/mL at week 4 of treatment.
VOSEVI (sofosbuvir/velpatasvir/voxilaprevir)

I. INDICATIONS

FDA-Approved Indications
Vosevi is indicated for the treatment of adult patients with chronic hepatitis C virus (HCV) infection without cirrhosis or with compensated cirrhosis (Child-Pugh A) who have:
A. Genotype 1, 2, 3, 4, 5, or 6 infection and have previously been treated with an HCV regimen containing an NS5A inhibitor
B. Genotype 1a or 3 infection and have previously been treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor

Additional benefit of Vosevi over sofosbuvir/velpatasvir was not shown in adults with genotype 1b, 2, 4, 5, or 6 infection previously treated with sofosbuvir without an NS5A inhibitor.

II. EXCLUSIONS
Decompensated cirrhosis/moderate or severe hepatic impairment (Child Turcotte Pugh Class B or C).

Note: When the requested drug is being used in a combination therapy regimen, exclusions to the other antiviral drugs also apply.

III. CRITERIA FOR APPROVAL

1. Chronic hepatitis C virus infection, without ribavirin
   1.1 Genotype 1a infection
       A. Authorization of up to 12 weeks total may be granted for members who failed prior treatment with a sofosbuvir-containing regimen without an HCV NS5A inhibitor.
       B. Authorization of up to 12 weeks total may be granted for members who failed prior treatment with an HCV NS5A inhibitor-containing regimen.

   1.2 Genotype 1b infection
       Authorization of up to 12 weeks total may be granted for members who failed prior treatment with an HCV NS5A inhibitor-containing regimen.

   1.3 Genotype 2 infection
       Authorization of up to 12 weeks total may be granted for members who failed prior treatment with an HCV NS5A inhibitor-containing regimen.

   1.4 Genotype 3 infection
       A. Authorization of up to 12 weeks total may be granted for members who failed prior treatment with any direct-acting antiviral regimen (eg, NS5A- or sofosbuvir-containing regimen).
       B. Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who are treatment naïve and have the Y93H substitution associated with velpatasvir resistance.
C. Authorization of up to 12 weeks total may be granted for members who failed prior treatment with PEG-IFN and RBV and meet one of the following:
  i. Member does not have cirrhosis and has the Y93H substitution associated with velpatasvir resistance.
  ii. Member has compensated cirrhosis.

1.5 Genotype 4, 5, or 6 infection
Authorization of up to 12 weeks total may be granted for members who failed prior treatment with any direct-acting antiviral regimen (eg, NS5A- or sofosbuvir-containing regimen)

2. Chronic hepatitis C virus infection, in combination with ribavirin
Genotype 3 infection
Authorization of up to 12 weeks total may be granted for members with cirrhosis who failed prior treatment with an HCV NS5A inhibitor-containing regimen.

3. HCV and HIV Coinfection
Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section III above are met.
MAVYRET (glecaprevir and pibrentasvir)

I. INDICATIONS

FDA-Approved Indications
Mavyret is indicated for the treatment of adult patients with chronic hepatitis C virus (HCV) genotype 1, 2, 3, 4, 5 or 6 infection without cirrhosis or with compensated cirrhosis (Child-Pugh A). Mavyret is also indicated for the treatment of adult patients with HCV genotype 1 infection, who previously have been treated with a regimen containing an HCV NS5A inhibitor or an NS3/4A protease inhibitor (PI), but not both.

II. EXCLUSIONS
Decompensated cirrhosis/moderate or severe hepatic impairment (Child Turcotte Pugh Class B or C)

Note: When the requested drug is being used in a combination therapy regimen, exclusions to the other antiviral drugs also apply.

III. CRITERIA FOR APPROVAL

1. Chronic hepatitis C virus infection
   1.1 Genotype 1 infection
   A. Authorization of up to 8 weeks total may be granted for treatment-naive members without cirrhosis.
   B. Authorization of up to 12 weeks total may be granted for treatment-naive members with compensated cirrhosis.
   C. Authorization of up to 16 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with an NS5A inhibitor and who has not received an NS3/4A protease inhibitor.
   D. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with an NS3/4A protease inhibitor (e.g., simeprevir, boceprevir or telaprevir in combination with peginterferon and ribavirin, simeprevir with sofosbuvir) and who have not received an NS5A inhibitor.
   E. Authorization of up to 8 weeks total may be granted for members without cirrhosis who failed prior treatment with peginterferon-alfa (PEG-IFN) and ribavirin (RBV) and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
   F. Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
G. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with a sofosbuvir (Sovaldi)-containing regimen (e.g., sofosbuvir and ribavirin with or without PEG-IFN) and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.

1.2 Genotype 2 infection
A. Authorization of up to 8 weeks total may be granted for treatment-naive members without cirrhosis.
B. Authorization of up to 12 weeks total may be granted for treatment-naive members with compensated cirrhosis.
C. Authorization of up to 8 weeks total may be granted for members without cirrhosis who failed prior treatment with PEG-IF and RBV and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
D. Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
E. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with sofosbuvir (Sovaldi) and ribavirin with or without PEG-IFN and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.

1.3 Genotype 3 infection
A. Authorization of up to 8 weeks total may be granted for treatment-naive members without cirrhosis.
B. Authorization of up to 12 weeks total may be granted for treatment-naive members with compensated cirrhosis.
C. Authorization of up to 16 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
D. Authorization of up to 16 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with sofosbuvir (Sovaldi) and RBV with or without PEG-IFN and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.

1.4 Genotype 4, 5, or 6 infection
A. Authorization of up to 8 weeks total may be granted for treatment-naive members without cirrhosis.
B. Authorization of up to 12 weeks total may be granted for treatment-naive members with compensated cirrhosis.
C. Authorization of up to 8 weeks total may be granted for members without cirrhosis who failed prior treatment with PEG-IFN and RBV and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
D. Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
E. Authorization of up to 8 weeks total may be granted for members without cirrhosis who failed prior treatment with sofosbuvir (Sovaldi) and ribavirin with or without
PEG-IFN and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.

F. Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with sofosbuvir (Sovaldi) and ribavirin with or without PEG-IFN and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.

1.5 Recurrent HCV infection post liver transplantation
Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis and recurrent HCV genotype 1, 2, 3, 4, 5 or 6 infection post liver transplantation.

1.6 Kidney transplant recipients
Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have HCV genotype 1, 2, 3, 4, 5 or 6 infection.

2. HCV and HIV Coinfection
Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section III above are met.

IX. Important Reminder

The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.

Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii’s Patients’ Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4), generally accepted standards of medical practice and review of medical literature and government approval status. HMSA has determined that services not covered under this Medical Policy will not be medically necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA’s determination as to medical necessity in a given case, the physician may request that HMSA reconsider the application of the medical necessity criteria to the case at issue in light of any supporting documentation.

X. References

plus sofosbuvir, with or without ribavirin, to treat chronic infection with hepatitis C virus genotype 1 in non-responders to pegylated interferon and ribavirin and treatment-naïve patients: the COSMOS randomized study. Lancet 2014; 384(9956): 1756-1765.


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