Preferred Regimen Based on Diagnosis:  
Mavyret™ (glecaprevir/pibrentasvir)

Non-Preferred:  
Daklinza® (daclatasvir)  
Epclusa® (sofosbuvir/velpatasvir)  
Harvoni® (sofosbuvir/ledipasvir)  
Olysio™ (simeprevir)  
Ribavirin  
Sovaldi® (sofosbuvir),  
Viekira™ PAK (ombitasvir, paritaprevir/ritonavir, dasabuvir)  
Vosevi™ (sofosbuvir, velpatasvir, voxilaprevir)  
Zepatier™ (elbasvir/grazoprevir)

Authorization Guidelines:  
For patients who meet all of the following (with submitted charts notes and lab results):

- Patient is of the appropriate age and/or weight for the drugs being requested per FDA labeling, National Treatment Guidelines or accepted reference compendia.
- Chronic Hepatitis C genotype 1, 2, 3, 4, 5 or 6
- Documentation of prescriber counseling regarding the risks of alcohol or IV drug abuse, and an offer of a referral for substance use disorder treatment when history of abuse is present.
- Baseline HCV-RNA within the last 3 months  
  - Documentation of the pretreatment state of hepatic fibrosis or cirrhosis (Fibrosis scores must be submitted, but no minimum value is required for approval. Only documentation of the disease severity is required.)
- Current treatment plan (see Monitoring), plan should include the following.
  - Documented commitment to adherence with the planned course of treatment and monitoring  
  - If the recipient has a history of failed treatment due to non-adherence, documentation that the cause of non-adherence have been corrected or addressed  
  - Documentation of counseling on how to reduce the risks for reinfection  
  - Provider agrees to submit HCV-RNA 3 months post treatment (SVR 12) regardless of the approved regimen.
- All potential drug interactions addressed by the prescriber (such as discontinuation of the interacting drug, dose reduction of the interacting drug, or counseling of the recipient of the risks associated with the use of both medications when they interact)
- Member has documented completion of:
  - Hepatitis B immunization series  
    OR
  - Hepatitis B screening (sAb/sAg and cAb/cAg)  
    AND
  - Quantitative HBV DNA if positive for hepatitis BsAg or cAb or cAg  
    AND
If there is detectable HBV DNA, will be treated for Hepatitis B
OR
If negative for hepatitis BsAb, is being vaccinated against Hepatitis B

- Member has documented HIV screening (HIV Ag/Ab) and if confirmed positive by HIV-1/HIV-2 differentiation immunoassay:
  - Is being treated for HIV
  OR
  - Is not being treated for HIV and the medical record documents the rationale for not being treated

AND
- If genotype 1a, or had a previous treatment failure with a direct-acting antiretroviral (DAA) regimen, is prescribed an AASLD recommended regimen based on the documented results of a NS5A RAS screening
- Request is for a preferred regimen

Additional Drug Criteria for Approval:
Mavyret is the preferred HCV agent and documentation will need to be provided to support the medical necessity of non-preferred agents if appropriate based on current AASLD guidance.

Mavyret™ (glecaprevir, pibrentasvir)
Member must meet the following:

- Member is treatment naïve and diagnosed with genotype 1, 2, 3, 4, 5, or 6 and meets one of the following:
  - Does not have cirrhosis; maximum duration of treatment is 8 weeks
  - With compensated cirrhosis (Child-Pugh A); maximum duration of treatment is 12 weeks

OR

- Member is treatment experienced and meets one of the following:
  - Genotype 1, member previously treated with an NS5A inhibitor (i.e., Harvoni, Daklinza) and not an NS3/4A inhibitor and does not have cirrhosis or with compensated cirrhosis (child-pugh A); maximum duration of treatment 16 weeks
  - Genotype 1, member previously treated with an NS3/4A inhibitor (i.e., Sov/Olysio, Olysio, Incivek, or Victrelis) and not an NS5A inhibitor and does not have cirrhosis or with compensated cirrhosis (Child-pugh A); maximum duration of treatment 12 weeks
  - Genotype 1,2,4,5, or 6 member was previously treated with an a PRS containing regimen (i.e., Peg/rbv ±Sov, sov/rbv) and one of the following:
    - Does not have cirrhosis; maximum duration of treatment 8 weeks (12 weeks in GT1 previously treated with a non-NS5A inhibitor, sofosbuvir-containing regimen)
    - With compensated cirrhosis (child-pugh A); maximum duration of treatment 12 weeks
- Genotype 3, member was previously treated with an a **PRS** containing regimen (i.e., Peg/rbv ±Sov, sov/rbv) and does not have cirrhosis or with compensated cirrhosis (child-pugh A); maximum duration of treatment 16 weeks
- Does not have severe liver impairment Child-Pugh C
- Will not be in used in combination with rifampin or atazanavir

*PRS (Peg/RBV and/or Sofosubuvir)*

**Treatment Naïve (TN):**

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Patient Population</th>
<th>Treatment</th>
<th>Duration of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,2,3,4,5,6</td>
<td>TN and No Cirrhosis</td>
<td>Mavyret</td>
<td>8 weeks</td>
</tr>
<tr>
<td>1,2,3,4,5,6</td>
<td>TN with compensated cirrhosis (Child-Pugh A)</td>
<td>Mavyret</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>

**Treatment Experienced (TE):**

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Patient Population</th>
<th>Treatment</th>
<th>Duration of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>TE with an NS5A inhibitor(^1) without an NS3/4A protease inhibitor (PI) No cirrhosis or with compensated cirrhosis (Child-Pugh A)</td>
<td>Mavyret</td>
<td>16 weeks</td>
</tr>
<tr>
<td>1</td>
<td>TE with an NS3/4A PI(^1) without an NS5A inhibitor No cirrhosis or with compensated cirrhosis (Child-Pugh A)</td>
<td>Mavyret</td>
<td>12 weeks</td>
</tr>
<tr>
<td>1,2,4,5, or 6</td>
<td>TE with PRS(^3) No cirrhosis</td>
<td></td>
<td>8 weeks</td>
</tr>
<tr>
<td>1,2,4,5, or 6</td>
<td>TE with PRS(^3) with compensated cirrhosis (Child-Pugh A)</td>
<td></td>
<td>12 weeks</td>
</tr>
<tr>
<td>3</td>
<td>TE with PRS(^3) no cirrhosis or with compensated cirrhosis (Child-Pugh A)</td>
<td></td>
<td>16 weeks</td>
</tr>
</tbody>
</table>

1. In clinical trials, subjects were treated with prior regimens containing ledipasvir and sofosbuvir or oclatasvir
with pegylated interferon and ribavirin.

2. In clinical trials, subjects were treated with prior regimens containing simeprevir and sofosbuvir, or simeprevir, boceprevir, or telaprevir with pegylated interferon and ribavirin.

3. PRS=Prior treatment experience with regimens containing interferon, pegylated interferon, ribavirin, and/or sofosbuvir, but no prior treatment experience with an HCV NS3/4A PI or NS5A inhibitor.

**Following Non-Preferred agents will be evaluated when above is contraindication or not indicated and the following drug specific criteria is met:**

**Zepatier** *(elbasvir/grazoprevir) genotype 1a or 1b and 4 HCV or HIV coinfection;*

Patient must meet the following:

- For genotype 1a - provide testing for NS5A Resistance Associated Variant (RAV); polymorphisms at position 28, 30, 31 or 93, requires a maximum duration of treatment of 16 weeks
- Patient does not have decompensated cirrhosis (Child Pugh B or C)
- Will not be in used in combination with the following medications (i.e., carbamazepine, phenytoin, rifampin, St. John’s Wort, cyclosporine, efavirenz, or HIV Protease Inhibitors)

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Patient Population</th>
<th>Treatment</th>
<th>Duration of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gt 1a</td>
<td>TN or TE (with PegIFN/RBV)</td>
<td>Zepatier</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td>Without baseline NS5A+ polymorphism</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>TN or TE with baseline NS5A polymorphism</td>
<td>Zepatier + RBV</td>
<td>16 weeks</td>
</tr>
<tr>
<td>Gt 1b</td>
<td>TN or TE (with PegIFN/RBV)</td>
<td>Zepatier</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Gt 1a or 1b</td>
<td>TE (with PegIFN/RBV and PI)</td>
<td>Zepatier + RBV</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>

*Patients with gt1a (+)NS5A RAV’s will require 16 weeks of treatment

<table>
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<tr>
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<th>Duration of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gt 4</td>
<td>TN</td>
<td>Zepatier</td>
</tr>
<tr>
<td></td>
<td>TE (with PegIFN/RBV)</td>
<td>Zepatier + RBV</td>
</tr>
</tbody>
</table>

TN=Treatment Naïve, TE=Treatment Experienced

‡Peginterferon alfa + ribavirin + HCV NS3/4A protease inhibitor

§The optimal ZEPATIER-based treatment regimen and duration of therapy for PegIFN/RBV/PI-experienced genotype 1a-infected patients with one or more baseline NS5A resistance-associated polymorphisms at positions 28, 30, 31 and 93 has not been established.

+NS5A polymorphism at positions 28, 30, 31 or 93

**Epclusa** *(sofosbuvir/velpatasvir)*

Patient must meet the following:
- For genotypes 2, 3, 5, or 6 without cirrhosis or compensated (Child-Pugh A) cirrhosis, the maximum duration of treatment is 12 weeks.
- For genotypes 1, 2, 3, 4, 5, or 6 with **decompensated** cirrhosis, Epclusa will be used in combination with ribavirin the maximum duration of treatment is 12 weeks.
- Will not be in used in combination with the following medications (i.e., amiodarone, carbamazepine, oxcarbazepine, phenytoin, rifampin, St. John’s Wort, tipranovir/ritonavir).
- Patient does not have eGFR < 30 ml/min or has ESRD requiring hemodialysis.

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<tr>
<th>Genotype</th>
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<th>Treatment</th>
<th>Duration of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gt 2, 3, 5 or 6</td>
<td>without cirrhosis or with compensated cirrhosis (Child-Pugh A)</td>
<td>Epclusa</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Gt 1, 2, 3, 4, 5 or 6</td>
<td>With <strong>decompensated</strong> cirrhosis (Child-Pugh B or C)</td>
<td>Epclusa + RBV</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>

**Vosevi ® (sofosbuvir, velpatasvir, voxilaprevir)**

Member must meet the following without cirrhosis or compensated cirrhosis (Child-Pugh A):

- Genotype 1, 2, 3, 4, 5, or 6, previously treated with an NS5A inhibitor (i.e., daclatasvir, elbasvir, ledipasvir, ombitasvir, velpatasvir) OR
- Genotype 1a or 3, previously treated with sofosbuvir without an NS5A inhibitor and with or without (i.e., peginterferon alfa/ribavirin, ribavirin, HCV NS3/4A PI (boceprevir, simeprevir or telaprevir)
- Will not exceed the maximum duration of treatment of 12 weeks
- Will not be in used in combination with rifampin
- Does not have eGFR < 30 ml/min or has ESRD requiring hemodialysis.

<table>
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<tr>
<th>Genotype</th>
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<th>Treatment</th>
<th>Duration of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1, 2, 3, 4, 5, 6</td>
<td>No cirrhosis or with compensated cirrhosis (child-Pugh A)</td>
<td>Vosevi</td>
<td>12 weeks</td>
</tr>
<tr>
<td>1a or 3</td>
<td>TE with an NS5A inhibitor(^a)</td>
<td>Vosevi</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>

\(^a\) In clinical trials, prior NS5A inhibitor experience included daclatasvir, elbasvir, ledipasvir, ombitasvir, or velpatasvir.
\(^b\) In clinical trials, prior treatment experience included sofosbuvir with or without any of the following: peginterferon alfa/ribavirin, ribavirin, HCV NS3/4A protease inhibitor (boceprevir, simeprevir or telaprevir).

Notes: 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.

**Harvoni® (ledipasvir/sofosbuvir)**

Patient must meet the following:

- For genotypes 1, 4, 5 and 6 treatment naïve or treatment experienced, liver transplant recipients with cirrhosis (Child Pugh A) or without cirrhosis; Harvoni will be used in combination with ribavirin the maximum duration of treatment is 12 weeks.
- Will not be in used in combination with the following medications (i.e., amiodarone, carbamazepine, oxcarbazepine, phenytoin, rifampin, St. John’s Wort, tipranovir/ritonavir)
- Patient does not have eGFR < 30 ml/min or has ESRD requiring hemodialysis

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<thead>
<tr>
<th>Genotype</th>
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<th>Treatment</th>
<th>Duration of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gt 1 or 4</td>
<td>TN or TE (with Peg/RBV ± PI) liver transplant recipients without cirrhosis or with compensated cirrhosis (Child-Pugh A)</td>
<td>Harvoni + RBV</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>

**Sovaldi® (sofosbuvir) in combination with ribavirin**

Patient must meet the following:
- Hepatocellular Carcinoma (awaiting transplantation)
  - Not previously transplanted AND
  - Must meet Milan criteria (defined as the presence of tumor 5 cm or less in diameter in patients with single hepatocellular carcinomas and no more than 3 tumor nodules, each 3 cm or less in diameter in patients with multiple tumors and no extra hepatic manifestations or evidence of vascular invasions of tumor)
  - Maximum duration of treatment 48 weeks
- Will not be in used in combination with the following medications (i.e., amiodarone, carbamazepine, oxcarbazepine, phenytoin, rifampin, St. John’s Wort, tipranovir/ritonavir)
- Patient does not have eGFR < 30 ml/min or has ESRD requiring hemodialysis

All other regimens not listed above will be considered on case by case basis according to the most current product labeling and AASLD guidelines.

**NON-Preferred Treatment Alternatives:**

a. Has a documented history of therapeutic failure, contraindication or intolerance to the preferred Hepatitis C Agents appropriate for the recipient’s genotype according to AASLD guidelines.

OR

b. Is currently receiving treatment with the same non-preferred Hepatitis C Agent (continuation of care from previous insurer).

**Monitoring:**

- Provider agrees to submit HCV-RNA week 12 and 3 months post treatment (SVR 12)
- Member understands treatment regimen and agrees to remain compliant and adherent during the full course of therapy.

**Initial Authorization:**

- Approval Duration – per treatment table as noted above.
Non-Coverage Criteria:

- Coverage for greater than the duration of treatment outlined in the table above
- Lifetime expectancy for less than 12 months due to non-liver related comorbid conditions
- Viekira, Viekira XR, Technivie, and Zepatier in patients with Child Pugh B or C
- Olysio, Daklinza and Sovaldi used as monotherapy
- Use in combination with other DAA’s unless indicated
- Any contraindications to any of the agents
  Non-FDA approved indications, which are not listed in Criteria for Approval section,, unless supported by the AASLD/IDSA National Treatment Guidelines.

Additional Information:

Ribavirin dosing recommendations and key contraindications:
- The daily dosage of ribavirin is weight-based (1000 mg for patients <75 kg and 1200 mg for those ≥75 kg) administered orally in two divided doses with food.
- For patients with decompensated cirrhosis or post-transplantation the recommended starting dose is 600mg once daily up to 1000 mg as tolerated
- Ribavirin is contraindicated in women who are pregnant or may become pregnant, including in men whose female partners are pregnant
- Ribavirin is contraindicated in patients with hemoglobinopathies (i.e, sickle cell anemia or thalassemia)

Case Management: Patient and prescriber agree to participate with nursing & pharmacy case management of the plan to assure patient compliance with the prescribed medication, access to services, lab tests, lab reviews and offer medical guidance as needed to optimize a successful outcome for the patient.

Response Definitions:

Partial Responder: Member experiences at least a 2-log10 (100 times) drop in HCV RNA, but has the inability to fully remove the virus from the blood by end of treatment.

Null/Non Responder: Member does not experience at least 2-log10 (100 times) drop in HCV RNA 8-12 weeks of treatment.

Relapser: Member has an undetectable HCV viral load at end of treatment regimen, but who has a detectable viral load within 12-24 weeks after stopping treatment.

References:
2. Harvoni [Prescribing Information]. Foster City, CA: Gilead Sciences, Inc.; Apr 2017
5. Olysio [Prescribing Information]. Titusville, NJ: Jansen.; Feb 2017
14. AASLD-IDSA. Recommendations for testing, managing, and treating hepatitis C.