PHARMACY PRIOR AUTHORIZATION
Hepatitis C Clinical Guideline

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

Note: Ribasphere is preferred and does not require a Prior Authorization (PA) if a Hepatitis C agent is approved

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

General Authorization Guidelines:

For members who meet ALL of the following (with submitted charts notes and lab results):
A. Request is for a preferred regimen
B. Diagnosis of chronic Hepatitis C with documented genotype
C. Member is of the appropriate age and/or weight for the drugs being requested per FDA labeling, National Treatment Guidelines or accepted reference compendia.
D. Member is prescribed a dose and length of therapy that is consistent with FDA-approved labeling or peer-reviewed medical literature
E. 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.
F. Baseline HCV-RNA within the last 3 months
G. 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.
H. Current treatment plan (see Monitoring), plan should include the following,
   1. Documented commitment to adherence with the planned course of treatment and monitoring
2. 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
3. Documentation of counseling on how to reduce the risks for reinfection
4. Provider agrees to submit HCV-RNA 3 months post treatment (SVR 12) 
regardless of the approved regimen.
5. Member does not have a life expectancy of less than 12 months due to non-
liver related comorbid conditions
I. 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)
J. Member has documentation of:
   1. A complete hepatitis B immunization series
      OR
   2. Hepatitis B screening (sAb/sAg and cAb)
      AND
   3. If positive for hepatitis B sAg, quantitative HBV DNA results
      AND
   4. If there is detectable HBV DNA, a treatment plan for hepatitis B consistent 
      with AASLD recommendations
      AND
   5. If negative for hepatitis B sAb, a hepatitis B immunization plan or counseling 
      to receive the hepatitis B immunization series
K. Member has documented HIV screening (HIV Ag/Ab) and if confirmed positive by 
   HIV-1/HIV-2 differentiation immunoassay:
      1. Is being treated for HIV
      OR
      2. Is not being treated for HIV and the medical record documents the rationale 
         for not being treated
L. 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

Additional Drug Specific Criteria:

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 OR Member is currently receiving treatment with a non-preferred Hepatitis C Agent (e.g. continuation of care from previous insurer).

**Mavyret™ (glecaprevir, pibrentasvir)**

Member must meet the following:

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

OR

B. Member is treatment experienced and meets ONE of the following:
   1. Genotype 1, member previously treated with an nonstructural protein 5A (NS5A) inhibitor (i.e., Harvoni, Daklinza) and an nonstructural protein S3/4A (NS3/4A) inhibitor, and does not have cirrhosis or with compensated cirrhosis (child-pugh A); maximum duration of treatment 16 weeks
   2. 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
   3. Genotype 1,2,4,5, or 6 member was previously treated with an a Peginterferon/ribavirin/sofosbuvir (PRS) containing regimen (i.e., Peg/rbv ±Sov, sov/rbv) and one of the following:
      i. Does not have cirrhosis; maximum duration of treatment 8 weeks (12 weeks in GT1 previously treated with a non-NS5A inhibitor, sofosbuvir-containing regimen)
      ii. With compensated cirrhosis (child-pugh A); maximum duration of treatment 12 weeks
   4. 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

C. Does not have severe liver impairment Child-Pugh C

D. Will not be in used in combination with rifampin or atazanavir
### 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></td>
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<tr>
<td></td>
<td>TN with compensated cirrhosis (Child-Pugh A)</td>
<td>Mavyret</td>
<td>8 weeks</td>
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<td></td>
<td></td>
<td></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 inhibitor¹ without an NS3/4A protease inhibitor (PI)</td>
<td></td>
<td>16 weeks</td>
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<td></td>
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<td></td>
<td></td>
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<tr>
<td></td>
<td>No cirrhosis or with compensated cirrhosis (Child-Pugh A)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>TE with an NS3/4A PI² without an NS5A inhibitor</td>
<td>Mavyret</td>
<td>12 weeks</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No cirrhosis or with compensated cirrhosis (Child-Pugh A)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>TE with PRS³</td>
<td></td>
<td>8 weeks</td>
</tr>
<tr>
<td>1, 2, 4, 5, or 6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>TE with PRS³ with compensated cirrhosis (Child-Pugh A)</td>
<td></td>
<td>12 weeks</td>
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<td></td>
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<tr>
<td></td>
<td>TE with a non-NS5A inhibitor, sofosbuvir-containing regimen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>TE with PRS³ 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 aclarasvir 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.
The following Non-Preferred agents will be evaluated when above is contraindicated or not indicated and the following drug specific criteria are met:

**Epclusa** *(sofosbuvir/velpatasvir)*  
Member must meet the following:  
A. For genotypes 1, 2, 3, 5, or 6 without cirrhosis or compensated (Child-Pugh A) cirrhosis, the maximum duration of treatment is 12 weeks  
B. 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  
C. Will not be in used in combination with the following medications (i.e., amiodarone, carbamazepine, oxcarbazepine, phenytoin, rifampin, St. John’s Wort, tipranovir/ritonavir)  
D. Does not have estimated glomerular filtration rate (eGFR) less than 30 ml/min or has end-stage renal disease (ESRD) requiring hemodialysis

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Patient Population</th>
<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>

**Harvoni®** *(ledipasvir/sofosbuvir)*  
Member must meet the following:  
A. 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  
B. Will not be in used in combination with the following medications (i.e., amiodarone, carbamazepine, oxcarbazepine, phenytoin, rifampin, St. John’s Wort, tipranovir/ritonavir)  
C. Patient does not have eGFR < 30 ml/min or has ESRD requiring hemodialysis

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Patient Population</th>
<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

Member must meet the following:

A. Hepatocellular Carcinoma (awaiting transplantation)
   1. Not previously transplanted AND
   2. 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)
   3. Maximum duration of treatment 48 weeks

B. Will not be in used in combination with the following medications (i.e., amiodarone, carbamazepine, oxcarbazepine, phenytoin, rifampin, St. John's Wort, tipranovir/ritonavir)

C. Patient does not have eGFR < 30 ml/min or has ESRD requiring hemodialysis

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

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

A. Genotype 1, 2, 3, 4, 5, or 6, previously treated with an NS5A inhibitor (i.e., daclatasvir, elbasvir, ledipasvir, ombitasvir, velpatasvir) OR

B. 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)

C. Will not exceed the maximum duration of treatment of 12 weeks

D. Will not be in used in combination with rifampin

E. Does not have eGFR < 30 ml/min or has ESRD requiring hemodialysis

<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>TE with an NS5A inhibitor(^a)</td>
<td>Vosevi</td>
<td>12 weeks</td>
</tr>
<tr>
<td>1a or 3</td>
<td>TE with Sofosbuvir without an NS5A inhibitor(^b)</td>
<td></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, HCVNS3/4A protease inhibitor (boceprevir, simeprevir or telaprevir).
Note: *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.*

**Zepatier® (elbasvir/grazoprevir)**

Member must meet the following:

A. 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
B. Member does not have decompensated cirrhosis (Child Pugh B or C)
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>
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<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>*Patients with gt1a (+)NS5A RAVs will require 16 weeks of treatment</td>
</tr>
<tr>
<td>Gt 4</td>
<td>TN</td>
<td>Zepatier</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td>TE (with PegIFN/RBV)</td>
<td>Zepatier + RBV</td>
<td>16 weeks</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

**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 and/or consistent with FDA-approved labeling or peer-reviewed medical literature

**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 and 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