Pharmacy Prior Authorization
Hepatitis C – Clinical Guideline

Viekira Pak/ XR® (ombitasvir, paritaprevir, ritonavir, dasabuvir)  Zepatier™ (elbasvir/grazoprevir)
Technivie® (ombitasvir, paritaprevir, ritonavir)  Harvoni® (sofosbuvir/ledipasvir)
Sovaldi® (sofosbuvir)  Daklinza™ (daclatasvir)
Vosevi™ (sofosbuvir, velpatasvir, voxilaprevir)  Epclusa® (glecaprevir/pibrentasvir)
Mavyret™ (glecaprevir/pibrentasvir)

Preferred Medication: Mavyret™

Note: Ribavirin tablets and capsules are preferred and do not require a Prior Authorization (PA) if a Hepatitis C agent is approved.

General Authorization Criteria:
For members 18 years of age or older who meet all of the following (with submitted charts notes, current medication list and lab results):

Note: For members ages 12+ please submit request for Harvoni

- Diagnosis of chronic Hepatitis C infection status confirmed by documentation of all of the following:
  - Detectable serum HCV RNA by quantitative assay completed within the past 90 days from the date of the prior authorization request
  - HCV genotype
  - Viral resistance status (when applicable)
  - Hepatic status (Child Pugh Score)
  - HCV viral load
- HCV treatment history and responses
- Prescribed by a physician specializing in infectious disease, gastroenterology, hepatology, or transplant
- Prescriber has submitted the following laboratory results which have been completed within the last 90 days:
  - Total bilirubin, albumin, and INR
  - Creatinine clearance or GFR
  - LFTs
  - CBC
  - Drug/alcohol screen
- Provider agrees to monitor hemoglobin levels periodically when a member is prescribed ribavirin
- Patient Readiness has been assessed and patient attestations of compliance is submitted and on file in member’s medical record
  - Prescribers shall use the Controlled Substances Prescription Monitoring Program [CSPMP] as a tool to aid in the review of compliance
- Member agrees to complete regimen and understands risks of reinfection and other contributors to liver disease and/or damage, through a signed attestation and agrees to participate in a treatment adherance program
- Prescribing clinician agrees to maintain HCV RNA levels obtained at 12 & 24-weeks post therapy completion to demonstrate Sustained Virilologic Response (SVR)
- Member has been screened for Hepatitis A and B, and shall have received at least one Hepatitis A, and at least one Hepatitis B vaccine prior to requesting treatment, unless member demonstrates laboratory evidence of immunity
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- Member shall be in remission for past three months from request date for treatment, and shall be engaged in a substance use disorder treatment program at time of prior authorization request, and over the course of treatment, if member has/had substance use disorder in past 12 months

- **If Retreatment**
  - Member was adherent to previous DAA therapy as evidenced by medical records and/or pharmacy prescription claims. If prior therapy was discontinued due to adverse effects from DAA, the medical record must be provided which documents these adverse effects and recommendation of discontinuation by treatment provider.
  - If member has substance use disorder in past 12 months from request date for treatment, member shall be in remission for past three months from request date for treatment, and shall be engaged in a substance use disorder treatment program at time of prior authorization request, and over the course of treatment, if DAA medications are approved
  - Member commits to documented planned course of treatment, including anticipated laboratory, imaging tests, and prescribing provider visits
  - Resistance-associated polymorphism testing, when applicable, has been completed and submitted with prior authorization request for regimens that the FDA requires testing, prior to treatment to ensure clinical appropriateness, and deemed medically necessary by clinical reviewer prior to approval of requested regimen.

- **Hepatitis C retreatment** will not be approved when:
  - Life expectancy is less than 12 months and cannot be remediated by treating the HCV infection, by transplantation, or by other directed therapy
  - Member was non-adherent to initial DAA treatment regimen as evidenced by medical records and/or pharmacy prescription claims
  - More than one retreatment with a DAA is requested. This is considered an experimental service as defined in A.A.C. R9-22-203. Based on current evidence, this includes more than one retreatment with a DAA and requested retreatment regimens that include more than one DAA

**Additional Drug Specific Criteria:**
Mavyret is the preferred hepatitis C virus (HCV) agent; documentation will need to be provided to support medical necessity of non-preferred agents.

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

- Member is treatment naïve (TN) 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 (TE) and meets one of the following:
  - Genotype 1, member previously treated with a nonstructural protein 5A (NS5A) inhibitor (i.e., Harvoni, Daklinza), and not a nonstructural protein 53/4A (NS3/4A) inhibitor, without cirrhosis, or with compensated cirrhosis (Child-Pugh A); maximum duration of treatment 16 weeks
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- Genotype 1, member previously treated with a nonstructural protein S3/4A (NS3/4A) inhibitor (i.e., Incivek, or Victrelis), and not a nonstructural protein 5A (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 a peginterferon/ribavirin/sofosbuvir (PRS) containing regimen only, and one of the following:
  - Without cirrhosis; maximum duration of treatment 8 weeks
  - With compensated cirrhosis (Child-Pugh A); maximum duration of treatment 12 weeks

- Genotype 3, member was previously treated with a peginterferon/ribavirin/sofosbuvir (PRS) containing regimen only, without cirrhosis, or with compensated cirrhosis (Child-Pugh A); maximum duration of treatment 16 weeks
  - Member does not have severe liver impairment Child-Pugh C
  - Mavyret will not be in used in combination with rifampin or atazanavir

### Treatment Naïve (TN):

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Member Population</th>
<th>Treatment</th>
<th>Duration of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,2,3,4,5,6</td>
<td>Treatment Naïve (TN) without cirrhosis</td>
<td>Mavyret</td>
<td>8 weeks</td>
</tr>
<tr>
<td></td>
<td>Treatment Naïve (TN) with compensated cirrhosis (Child-Pugh A)</td>
<td></td>
<td>12 weeks</td>
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### Treatment Experienced (TE):

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Member Population</th>
<th>Treatment</th>
<th>Duration of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Treatment Experienced (TE) with an nonstructural protein 5A (NS5A) inhibitor without an nonstructural protein S3/4A (NS3/4A) protease inhibitor (PI) Without cirrhosis or with compensated cirrhosis (Child-Pugh A)</td>
<td>Mavyret</td>
<td>16 weeks</td>
</tr>
<tr>
<td></td>
<td>Treatment Experienced (TE) with an NS3/4A protease inhibitor (PI) without an nonstructural protein 5A (NS5A) inhibitor No cirrhosis or with compensated cirrhosis (Child-Pugh A)</td>
<td></td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td>Treatment Experienced (TE) with peginterferon/ribavirin/sofosbuvir</td>
<td></td>
<td>8 weeks</td>
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</tbody>
</table>
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1. In clinical trials, subjects were treated with prior regimens containing ledipasvir and sofosbuvir or daclatasvir 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 hepatitis C virus (HCV) nonstructural protein S3/4A (NS3/4A) protease inhibitor (PI) or nonstructural protein 5A (NS5A) inhibitor.

Epclusa (sofosbuvir/velpatasvir)
- Nonstructural protein 5A (NS5A) resistance-associated substitutions (RAS) testing is required for genotype 3-infected, treatment-experienced members (with or without cirrhosis), and treatment-naive members with cirrhosis being considered for 12 weeks of sofosbuvir/velpatasvir. If Y93H is present, weight-based ribavirin (RBV) should be added.

Member must meet the following:
- For genotypes 1, 2, 3, 4, 5, or 6 with decompensated cirrhosis, Epclusa will be used in combination with ribavirin (RBV) the maximum duration of treatment is 12 weeks
- For genotypes 1, 2, 3, 4, 5, or 6 without cirrhosis or compensated cirrhosis (Child-Pugh A), 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, tipranavir/ritonavir)
- 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>Member Population</th>
<th>Treatment</th>
<th>Duration of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1, 2, 3, 4, 5 or 6</td>
<td>Treatment Naive (TN) and Epclusa</td>
<td>12 weeks</td>
<td></td>
</tr>
</tbody>
</table>
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<tr>
<th>Genotype</th>
<th>Member Population</th>
<th>Treatment</th>
<th>Duration of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1, 2, 3, 4, 5, 6</td>
<td>Treatment Experienced (TE) with a nonstructural protein 5A (NS5A) inhibitor (i.e., daclatasvir, elbasvir, ledipasvir, ombitasvir, velpatasvir) without cirrhosis or with compensated cirrhosis (Child-Pugh A)</td>
<td>Vosevi</td>
<td>12 weeks</td>
</tr>
<tr>
<td>1a or 3</td>
<td>Treatment Experienced (TE) with Sofosbuvir without a nonstructural protein 5A (NS5A) inhibitor without cirrhosis or with compensated cirrhosis (Child-Pugh A)</td>
<td>Epclusa + ribavirin (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 nonstructural protein 5A (NS5A) inhibitor (i.e., daclatasvir, elbasvir, ledipasvir, ombitasvir, velpatasvir) OR
- Genotype 1a or 3, previously treated with sofosbuvir without an nonstructural protein 5A (NS5A) inhibitor and with or without (i.e., peginterferon/ribavirin (RBV), ribavirin (RBV), hepatitis C virus (HCV) nonstructural protein S3/4A (NS3/4A) Protease Inhibitor (PI) (i.e. boceprevir, simeprevir or telaprevir)
- Will not exceed the maximum duration of treatment of 12 weeks
- Vosevi will not be in used in combination with rifampin
- Does not have eGFR less than 30 ml/min or has ESRD requiring hemodialysis

a. In clinical trials, prior nonstructural protein 5A (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, hepatitis C virus (HCV) nonstructural protein S3/4A (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 nonstructural protein 5A (NS5A) inhibitor.
Zepatier (elbasvir/grazoprevir)

Member must meet the following:

- For genotype 1a testing is required for nonstructural protein 5A (NS5A) resistance-associated substitutions (RAS); polymorphisms at position 28, 30, 31 or 93, requires a maximum duration of treatment of 16 weeks
- Member does not have decompensated cirrhosis (Child-Pugh B or C)
- Zepatier 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>Member Population</th>
<th>Treatment</th>
<th>Duration of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>Treatment Naïve (TN) or Treatment Experienced (TE) (with PegIFN/ribavirin (RBV)) Without baseline nonsructural protein 5A (NS5A) polymorphism</td>
<td>Zepatier</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td>Treatment Naïve (TN) or Treatment Experienced (TE) with baseline nonsructural protein 5A (NS5A) polymorphism</td>
<td>Zepatier + ribavirin (RBV)</td>
<td>16 weeks</td>
</tr>
<tr>
<td>1b</td>
<td>Treatment Naïve (TN) or Treatment Experienced (TE) (with PegIFN/RBV)</td>
<td>Zepatier</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>
| 1a§ or 1b| Treatment Experienced (TE) (with PegIFN/ribavirin (RBV) and protease inhibitor (PI)†) | Zepatier + ribavirin (RBV) | 12 weeks
*Patients with gt1a (+)NS5A RAV’s will require 16 weeks of treatment |
| 4        | Treatment Naïve (TN) | Zepatier | 12 weeks |
|          | Treatment Experienced (TE) (with PegIFN/ribavirin (RBV)) | Zepatier + ribavirin (RBV) | 16 weeks |

†Peginterferon alfa + ribavirin + hepatitis C virus (HCV) nonstructural protein 53/4A (NS3/4A) protease inhibitor (PI)

§The optimal ZEPATIER-based treatment regimen and duration of therapy for PegIFN/ribavirin (RBV)/PI-experienced genotype 1a-infected patients with one or more baseline nonsructural protein 5A (NS5A) resistance-associated polymorphisms at positions 28, 30, 31 and 93 has not been established.

† nonstructural protein 5A (NS5A) polymorphism at positions 28, 30, 31 or 93

Harvoni (ledipasvir/sofosbuvir)

Member is 12 years of age or older weighing at least 35 kg and meets the following:
- For genotypes 1, 4, 5, or 6
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- Will not be in used in combination with the following medications (i.e., amiodarone, carbamazepine, oxcarbazepine, phenytoin, rifampin, St. John’s Wort, tipranavir/ritonavir)
- Member does not have eGFR less than 30 ml/min or has ESRD requiring hemodialysis

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<tr>
<th>Genotype</th>
<th>Member Population</th>
<th>Treatment</th>
<th>Duration of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Treatment Naïve (TN) without cirrhosis (with pretreatment HCV RNA less than 6 million IU/ml)</td>
<td>Harvoni</td>
<td>8 weeks</td>
</tr>
<tr>
<td></td>
<td>Treatment Naïve (TN) without cirrhosis or with compensated cirrhosis (Child-Pugh A)</td>
<td>Harvoni</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td>Treatment Experienced (TE) (PegIFN/ribavirin (RBV)± protease inhibitor (PI)) without cirrhosis</td>
<td>Harvoni</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td>Treatment Experienced (TE) (PegIFN/ribavirin (RBV)± protease inhibitor (PI)) with compensated cirrhosis (Child-Pugh A)</td>
<td>Harvoni</td>
<td>24 weeks</td>
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<tr>
<td></td>
<td>Harvoni + ribavirin (RBV) (If eligible for RBV)</td>
<td>Harvoni + ribavirin (RBV)</td>
<td>12 weeks</td>
</tr>
<tr>
<td>1 or 4</td>
<td>Treatment Naïve (TN) and Treatment Experienced (TE) (PegIFN/RBV± protease inhibitor (PI)) with decompensated cirrhosis (Child-Pugh B or C)</td>
<td>Harvoni + ribavirin (RBV)</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td>Treatment Naïve (TN) or Treatment Experienced (TE) (PegIFN/RBV± protease inhibitor (PI)) without or with compensated cirrhosis (Child-Pugh A)</td>
<td>Harvoni</td>
<td>12 weeks</td>
</tr>
<tr>
<td>4, 5, or 6</td>
<td>Treatment Naïve (TN) and Treatment Experienced (TE) (PegIFN/ribavirin (RBV)± protease inhibitor (PI)) without cirrhosis or with compensated cirrhosis (Child-Pugh A)</td>
<td>Harvoni</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>
** TE with Peg/RBV ± PI

Children (12 years of age and older or weighing at least 35 kg)

<table>
<thead>
<tr>
<th>Genotype</th>
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<th>Treatment</th>
<th>Duration of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Treatment Naïve (TN) without or with compensated cirrhosis (Child-Pugh A)</td>
<td>Harvoni</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td>Treatment Experienced (TE) without cirrhosis</td>
<td>Harvoni</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td>Treatment Experienced (TE) with compensated cirrhosis (Child-Pugh A)</td>
<td>Harvoni</td>
<td>24 weeks</td>
</tr>
<tr>
<td>4, 5 or 6</td>
<td>Treatment Naïve (TN) or Treatment Experienced (TE) without or with compensated cirrhosis (Child-Pugh A)</td>
<td>Harvoni</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>

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

Member 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 members with single hepatocellular carcinomas and no more than 3 tumor nodules, each 3 cm or less in diameter in members with multiple tumors and no extra hepatic manifestations or evidence of vascular invasions of tumor)
  - Maximum treatment duration of 48 weeks
- Will not be in used in combination with the following medications (i.e., amiodarone, carbamazepine, oxicarbazepine, phenytoin, rifampin, St. John’s Wort, tipranavir/ritonavir)
- Member does not have eGFR less than 30 ml/min or has ESRD requiring hemodialysis

All other regimens not listed above will be considered on case by case bases

**Non-Coverage Criteria:**
- Direct Acting Antiviral dosages greater than the FDA approved maximum dosage
- Coverage for greater than the duration of treatment outlined in the tables within the guideline
- Lost or stolen medication or fraudulent use
- Lifetime expectancy for less than 12 months due to non-liver related comorbid conditions
- Viekira Pak, Viekira XR, and Technivie, in member’s with Child-Pugh B or C
- Zepatier if the NS5A Polymorphism testing has not been completed and submitted with the prior authorization request
- Daklinza and Sovaldi used as monotherapy
- Members when there is documented non-adherence to prior HCV medications, HCV medical treatment, or failure to complete HCV disease evaluation appointments and laboratory and imaging procedures
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- Members declining to participate in a treatment adherence program
- Members declining to participate in a substance abuse disorder treatment program
- Members currently using a P-gp inducer drug (St. John’s wort, rifampin, carbamazepine, ritonavir, tipranavir etc.),
- Use in combination with other direct-acting antivirals (DAAs) unless indicated
- Any contraindications to any of the agents

Initial Authorization:
- Approve for the full course of therapy

Additional Information:

Hep B Reactivation:
Per AASLD: All members initiating hepatitis C virus (HCV) direct-acting antivirals (DAA) therapy should be assessed for HBV coinfection with testing for hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (anti-HBs), and hepatitis b core antibodies (anti-HBc). HBV vaccination is recommended for all susceptible individuals.

Ribavirin dosing recommendations and key contraindications:
- The daily dosage of ribavirin is weight-based (1000 mg for members less than 75 kg and 1200 mg for those greater than or equal to 75 kg) administered orally in two divided doses with food
- For members with decompensated cirrhosis or post-transplantation, the recommended starting dose is 600mg/day (in two divided doses) increased monthly by 200mg to a weight-based dosing of 1200mg/day for members more than 75kg and 1000mg/day for members 75kg or less in two divided doses with food
- Ribavirin is contraindicated in women who are pregnant or may become pregnant, including in men whose female partners are pregnant
- Ribavirin is contraindicated in members with hemoglobinopathies (i.e., sickle-cell anemia or thalassemia)

HIV and hepatitis C virus (HCV) Drug interactions/links:


http://www.hep-druginteractions.org/

https://www.hcvguidelines.org/evaluate/resistance

Response Definitions:
- Partial Responder: Member experiences at least a 2-log10 (100 times) drop in hepatitis C virus ribonucleic acid (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 hepatitis C virus ribonucleic acid (HCV-RNA) 8-12 weeks of treatment.

Last Update: 6/2019
• **Relapse:** Member has an undetectable hepatitis C virus (HCV) viral load at end of treatment regimen, but who has a detectable viral load within 12-24 weeks after stopping treatment.

**Cirrhosis and Fibrosis Definitions:**
- Fibrosis: histological consequence (activation of hepatic stellate cells) of wound-healing process, which results in a net imbalance of collagen fiber synthesis and decomposition
- Cirrhosis: always developed from fibrosis, cirrhosis is an advanced stage of liver fibrosis with distortion in the hepatic vasculature (i.e. portal hypertension) and structure (i.e. abnormal lobules)
  - Compensated: varices present
  - Decompensated: development of ascites, variceal hemorrhage, encephalopathy, and/or jaundice

<table>
<thead>
<tr>
<th>Metavir</th>
<th>Fibrosis</th>
</tr>
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<tbody>
<tr>
<td>F0</td>
<td>No fibrosis</td>
</tr>
<tr>
<td>F1</td>
<td>Portal fibrosis without septa</td>
</tr>
<tr>
<td>F2</td>
<td>Septal fibrosis (portal-portal)</td>
</tr>
<tr>
<td>F3</td>
<td>Septal fibrosis (portal-central)</td>
</tr>
<tr>
<td>F4</td>
<td>Compensated cirrhosis</td>
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<tr>
<td></td>
<td>Decompensated cirrhosis</td>
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</tbody>
</table>

**References:**