Aetna Better Health®
Pharmacy Prior Authorization
Hepatitis C – Clinical Guideline

Viekira Pak/ XR® (ombitasvir, paritaprevir, ritonavir, dasabuvir)
Technivie® (ombitasvir, paritaprevir, ritonavir)
Olysio® (simeprevir)
Epclusa® (sofosbuvir/velpatasvir)
Vosevi™ (sofosbuvir, velpatasvir, voxilaprevir)

Zepatier™ (elbasvir/grazoprevir)
Harvoni® (sofosbuvir/ledipasvir)
Sovaldi® (sofosbuvir)
Daklinza™ (daclatasvir)
Mavyret™ (glecaprevir/pibrentasvir)

Preferred Medication: Mavyret™

Note: Ribasphere is preferred and does 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 and lab results):
- Diagnosis of Chronic Hepatitis C for genotype 1, 2, 3, 4, 5, and 6
- Prescribed by a physician specializing in infectious disease, gastroenterology, hepatology, or transplant
- Documentation of prescriber counseling regarding the risks of alcohol or intravenous (IV) drug abuse, and an offer of a referral for substance use disorder treatment when history of abuse is present
- Baseline hepatitis C virus ribonucleic acid (HCV-RNA) within the last 3 months
- Monitoring treatment plan which includes the following:
  - Provider agrees to submit hepatitis C virus ribonucleic acid (HCV-RNA) at treatment week 4 and 12 weeks post treatment
  - Provider asserts member is ready for treatment and understands treatment regimen and agrees to remain compliant and adherent during the full course of therapy
  - The prescriber must certify that the treatment will be discontinued if the viral load is detectable at week four of treatment and has increased by greater than 10-fold (greater than 1 log10 IU/mL) on repeat testing at week six
- Member has been screened for Hepatitis B virus (HBV) within the previous year and HBV status is addressed appropriately:
  - HBV negative: If not previously vaccinated, vaccination has been initiated or there is a plan to initiate (if not contraindicated)
  - HBV positive/history of HBV positive: Will place on suppressive therapy or monitor for reactivations as is appropriate

Additional Drug Specific Criteria:
Mavyret is the preferred hepatitis C virus (HCV) agent; documentation will need to be provided to support the 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:
  o Genotype 1, member previously treated with a nonstructural protein 5A (NS5A) inhibitor (i.e., Harvoni, Daklinza) and not a nonstructural protein S3/4A (NS3/4A) inhibitor, without cirrhosis or with compensated cirrhosis (Child-Pugh A); maximum duration of treatment 16 weeks
  o Genotype 1, member previously treated with a nonstructural protein S3/4A (NS3/4A) inhibitor (i.e., Sov/Olysio, Olysio, 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
  o 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
  o 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
  ▪ Does not have severe liver impairment Child-Pugh C
  ▪ 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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</table>

### 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 a nonstructural protein 5A (NS5A) inhibitor without an nonstructural protein S3/4A (NS3/4A) protease inhibitor (PI)</td>
<td></td>
<td>16 weeks</td>
</tr>
<tr>
<td>Without cirrhosis or with compensated cirrhosis (Child-Pugh A)</td>
<td>Mavyret</td>
<td>12 weeks</td>
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<tr>
<td>Treatment Experienced (TE) with an NS3/4A protease inhibitor (PI)(^2) without an nonstructural protein 5A (NS5A) inhibitor</td>
<td>Mavyret</td>
<td>12 weeks</td>
<td></td>
</tr>
<tr>
<td>No cirrhosis or with compensated cirrhosis (Child-Pugh A)</td>
<td>8 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1, 2, 4, 5, or 6</td>
<td>Treatment Experienced (TE) with peginterferon/ribavirin/sofosbuvir (PRS)(^3)</td>
<td>8 weeks</td>
<td></td>
</tr>
<tr>
<td>Without cirrhosis</td>
<td>Treatment Experienced (TE) with peginterferon/ribavirin/sofosbuvir (PRS)(^3) with compensated cirrhosis (Child-Pugh A)</td>
<td>12 weeks</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Treatment Experienced (TE) with peginterferon/ribavirin/sofosbuvir (PRS)(^3) without cirrhosis or with compensated cirrhosis (Child-Pugh A)</td>
<td>16 weeks</td>
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</tr>
</tbody>
</table>

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 an 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 Treatment Experienced (TE) (Peg/ribavirin (RBV) ± NS3 protease inhibitor (PI)) without cirrhosis or with compensated cirrhosis (Child-Pugh A)</td>
<td>Epclusa</td>
<td>12 weeks</td>
</tr>
<tr>
<td>1, 2, 3, 4, 5 or 6</td>
<td>Treatment Naive (TN) and Treatment Experienced (TE) (Peg/ribavirin (RBV) ± NS3 protease inhibitor (PI)) With decompensated cirrhosis (Child-Pugh B or C)</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
- Will not be in used in combination with rifampin
- Does not have eGFR less than 30 ml/min or has ESRD requiring hemodialysis

<table>
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<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 an NS5A inhibitor 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 an nonstructural</td>
<td>Vosevi</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>
protein 5A (NS5A) inhibitor\(^b\) without cirrhosis or with compensated cirrhosis (Child-Pugh A)

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)
- 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 nonstructural protein 5A (NS5A)(^+) polymorphism</td>
<td>Zepatier</td>
<td>12 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>
<tr>
<td>1a(\approx) 1b</td>
<td>Treatment Experienced (TE) (with PegIFN/ribavirin (RBV) and protease inhibitor (PI)(\approx))</td>
<td>Zepatier + ribavirin (RBV)</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>*Patients with gt1a (+)NS5A RAV's will require 16 weeks of treatment</td>
</tr>
<tr>
<td>4</td>
<td>Treatment Naïve (TN)</td>
<td>Zepatier</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td>Treatment Experienced (TE) (with</td>
<td>Zepatier +</td>
<td>16 weeks</td>
</tr>
</tbody>
</table>
‡Peginterferon alfa + ribavirin + hepatitis C virus (HCV) nonstructural protein S3/4A (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 nonstructural 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
- 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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<th>Member Population</th>
<th>Treatment</th>
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<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)</td>
<td>12 weeks (If eligible for RBV)</td>
<td></td>
</tr>
<tr>
<td></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</td>
<td>Harvoni</td>
<td>12 weeks</td>
</tr>
</tbody>
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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, oxcarbazepine, 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:
- 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, Technivie, and Zepatier in member’s with Child-Pugh B or C
- Olysio, Daklinza and Sovaldi used as monotherapy
- 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

Case Management: For plans that support hepatitis C virus (HCV) the following will be required:
Member and prescriber agree to participate with nursing and pharmacy case management of the plan to assure member 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 member.

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.
- **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>
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<tbody>
<tr>
<td>F0</td>
<td>No fibrosis</td>
</tr>
<tr>
<td>Non-Cirrhosis Stage of Chronic Liver Disease</td>
<td></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>
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<tr>
<td>Cirrhotic Stage of Chronic Liver Disease</td>
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</tr>
<tr>
<td>F4</td>
<td>Compensated cirrhosis</td>
</tr>
<tr>
<td></td>
<td>Decompensated cirrhosis</td>
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</tbody>
</table>

References: