Aetna Better Health®

Pharmacy Prior Authorization
Hepatitis C – Clinical Guideline

Preferred Medication:
Mavyret™ (glecaprevir/pibrentasvir)

Nonpreferred Medications:
Viekira Pak/XR® (ombitasvir, paritaprevir, ritonavir, dasabuvir), Zepatier™ (elbasvir/grazoprevir),
Technivie® (ombitasvir, paritaprevir, ritonavir), Harvoni® (sofosbuvir/ledipasvir), Sovaldi® (sofosbuvir),
Epclusa® (sofosbuvir/velpatasvir), Vosevi™ (sofosbuvir, velpatasvir, voxilaprevir)

Note: sofosbuvir/velpatasvir will be authorized for treatment-naïve and treatment-experienced members,
with decompensated cirrhosis (Child-Pugh B and C) in combination with ribavirin for a duration of 12 weeks

Note: ribavirin 200 mg capsule and 200 mg tablet are preferred and do not require a Prior Authorization if
a Hepatitis C agent is approved

General Authorization Criteria:
• Member meets all the following criteria (Along with submitted documentation of charts notes and lab
  results):
  o Age is 12 years of age or older, or weight is greater than or equal to 45 kilograms
  o Fibrosis score (Note: Fibrosis score F0-F4 is eligible for treatment)
  o Baseline hepatitis C virus ribonucleic acid (HCV-RNA) within the last 3 months
    o If newly diagnosed with Hepatitis C infection within the past year, 2 hepatitis C virus ribonucleic
      acid (HCV-RNA) levels must be taken at least 6 months apart to demonstrate a chronic
      Hepatitis C Virus infection.
  o Diagnosis of Chronic Hepatitis C
  o Documentation of hepatitis C virus (HCV) genotype
    NOTE: Not required for requests for a preferred first-line treatment regimen for members meeting
    simplified treatment eligibility
  o Prescribed by, or in consultation with a gastroenterologist, hepatologist, infectious disease, HIV
    Specialist (American Academy of HIV Medicine - AAHIVS) or transplant specialist or for the
    following circumstances:
    o Previous Hepatitis C treatment
    o Cirrhosis (as suggested by Fibrosis-4 (FIB-4) score greater than 3.25 or evidenced by a
      proprietary serologic test, transient elastography, prior liver biopsy or other clinical findings
      suggestive of liver dysfunction)
    o HIV (Human Immunodeficiency Virus) or Hepatitis B Surface Antigen (HBsAg) positive
    o Current pregnancy
    o Known or suspected hepatocellular carcinoma
    o Prior Liver transplantation
      NOTE: No prescriber restrictions for requests for a preferred first-line treatment regimen for
      members meeting simplified treatment eligibility

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Member has been screened for HIV (Human Immunodeficiency Virus) antigen/antibody test to determine simplified treatment eligibility

Member has been screened for Hepatitis B virus (HBV) within previous year to determine simplified treatment eligibility, and Hepatitis B virus (HBV) status is addressed appropriately

**Direct-Acting Antiviral Therapy Retreatment** (requests for repeat direct-acting antiviral therapy will be considered on a case by case basis):

- All the following additional criteria will apply:
  - Prescriber must answer all the following questions:
    - Is retreatment necessary due to treatment failure or reinfection?
    - Was member adherent (for example, few to no missed doses) with previous direct-acting antiviral therapy? If not, why?
    - Were there any additional factors that led to direct-acting antiviral therapy treatment failure? If so, describe these factors, and how they have been addressed, or are no longer relevant.
  - Member must be evaluated for alcohol, and substance abuse using a validated screening tool
  - For recent history (within the past 6 months) of alcohol, or substance abuse, the following criteria is required:
    - Documentation member completed, or is participating in recovery program, receiving alcohol, or substance abuse counseling services, or seeing an addiction specialist as part of Hepatitis C Virus treatment
    - Documentation member is not actively participating in illicit substance use, or alcohol abuse with confirmatory laboratory testing such as urine drug screen
  - Prescriber attests to all the following:
    - Member is willing and able to comply with requirements of proposed retreatment plan
    - Any factors that may have led to nonadherence with previous treatment(s) have been addressed
    - Member has received education regarding risk behaviors (for example, intravenous drug use) associated with Hepatitis C Virus infection).

**Non-Coverage Criteria:**

- Coverage for greater than duration of treatment outlined in 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 members with Child-Pugh B or C
- Use in combination with other direct-acting antivirals (DAAs) unless indicated
- Any contraindications to any of the agents

**Additional Criteria:**

Mavyret is the preferred Hepatitis C Virus agent; documentation to support medical necessity of non-preferred agents is required.

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

- Treatment naïve
  - One of the following is present:
    - No cirrhosis; maximum treatment duration 8 weeks
    - Compensated cirrhosis (Child-Pugh A) maximum treatment duration 8 weeks
    OR
  - Treatment experienced
    - One of the following is present:
      - Genotype 1
        - Previously treated with a Non-Structural Protein 5A (NS5A) inhibitor (for example, Harvoni, Daklinza), and not a Non-Structural Protein S3/4A (NS3/4A) inhibitor
        - No cirrhosis or compensated cirrhosis (Child-Pugh A); maximum treatment duration 16 weeks
      - Genotype 1
        - Previously treated with a Non-Structural Protein S3/4A (NS3/4A) inhibitor (for example, Sovaldi/Olysio, Olysio, Incivek, or Victrelis) and not a Non-Structural Protein 5A (NS5A) inhibitor
        - No cirrhosis or compensated cirrhosis (Child-Pugh A); maximum treatment duration 12 weeks
      - Genotype 1, 2, 4, 5, or 6
        - Previously treated with a peginterferon/ribavirin/sofosbuvir containing regimen only, and one of the following:
          - No cirrhosis; maximum treatment duration 8 weeks
          - Compensated cirrhosis (Child-Pugh A); maximum treatment duration 12 weeks
      - Genotype 3
        - Previously treated with a peginterferon/ribavirin/sofosbuvir containing regimen only
        - No cirrhosis or compensated cirrhosis (Child-Pugh A); maximum treatment duration 16 weeks

- There is no severe liver impairment Child-Pugh C
- Will not be in used in combination with potent P-Gp/CYP3A inducer drug (St. John’s wart, phenytoin, rifampin or, carbamazepine, efavirenz,) or atazanavir, ritonavir, tipranavir, etc.

### Treatment Naïve:

<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 without cirrhosis</td>
<td></td>
<td>8 weeks</td>
</tr>
</tbody>
</table>
### Treatment Naïve with compensated cirrhosis (Child-Pugh A)

- **Treatment**: Mavyret
- **Duration**: 8 weeks

### Treatment Experienced:

<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 with a Non-Structural Protein 5A (NS5A) inhibitor(^1) without a Non-Structural Protein 3/4A (NS3/4A) protease inhibitor No cirrhosis or compensated cirrhosis (Child-Pugh A)</td>
<td>Mavyret</td>
<td>16 weeks</td>
</tr>
<tr>
<td></td>
<td>Treatment Experienced with a NS3/4A Protease Inhibitor(^2) without a Non-Structural Protein 5A (NS5A) inhibitor No cirrhosis or compensated cirrhosis (Child-Pugh A)</td>
<td></td>
<td>12 weeks</td>
</tr>
<tr>
<td>1, 2, 4, 5, or 6</td>
<td>Treatment Experienced with peginterferon/ribavirin/sofosbuvir(^3) No cirrhosis</td>
<td></td>
<td>8 weeks</td>
</tr>
<tr>
<td></td>
<td>Treatment Experienced with peginterferon/ribavirin/sofosbuvir(^3) Compensated cirrhosis (Child-Pugh A)</td>
<td></td>
<td>12 weeks</td>
</tr>
<tr>
<td>3</td>
<td>Treatment Experienced with peginterferon/ribavirin/sofosbuvir(^3) No cirrhosis or compensated cirrhosis (Child-Pugh A)</td>
<td></td>
<td>16 weeks</td>
</tr>
</tbody>
</table>

### Liver or Kidney Transplant Recipients:
- Standard recommended duration 12 weeks

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Member Population</th>
<th>Treatment</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>1, 3</td>
<td>Genotype 1</td>
<td>Mavyret</td>
<td>16 weeks</td>
</tr>
</tbody>
</table>
Treatment experienced with a Non-Structural Protein 5A (NS5A) inhibitor without prior treatment with a Non-Structural Protein S3/4A (NS3/4A) OR Genotype 3
• Treatment experienced with regimens containing peginterferon, ribavirin, and/or sofosbuvir

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 a hepatitis C virus (HCV) nonstructural protein S3/4A (NS3/4A) protease inhibitor (PI) or nonstructural protein 5A (NS5A) inhibitor.

Initial Authorization:
• Approve for the full course of therapy
• All request must be sent to Medical Director for final determination

Additional Information:

Hepatitis B Reactivation: Per the American Association for the Study of Liver Disease (AASLD): All members initiating hepatitis C virus (HCV) direct-acting antivirals (DAA) therapy should be assessed for hepatitis B virus (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:
• 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, 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 (for example, sickle-cell anemia or thalassemia)

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HIV and hepatitis C virus (HCV) Drug interactions/links:
- [https://www.hcvguidelines.org/evaluate/resistance](https://www.hcvguidelines.org/evaluate/resistance)

Case Management:
- For plans that support hepatitis C virus the following will be required:
  - Member and prescriber agree to participate with nursing, and pharmacy case management of the plan, to assure compliance with prescribed medication, access to services, lab tests, lab reviews and offer medical guidance as needed to optimize successful outcome.

Response Definitions:
- **Partial Responder:**
  - Member experiences at least a 2-log10 (100 times) drop in hepatitis C virus ribonucleic acid (HCV-RNA) but has inability to fully remove virus from 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 undetectable hepatitis C virus viral load at end of treatment regimen but has 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 net imbalance of collagen fiber synthesis and decomposition.
- **Cirrhosis:**
  - Always developed from fibrosis, cirrhosis is an advanced stage of liver fibrosis with distortion in hepatic vasculature (for example portal hypertension) and structure (for example, abnormal lobules)
    - Compensated: Varices present
    - Decompensated: Development of ascites, variceal hemorrhage, encephalopathy, and/or jaundice

<table>
<thead>
<tr>
<th>Non-Cirrhosis Stage of Chronic Liver Disease</th>
<th>Metavir</th>
<th>Fibrosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>F0</td>
<td>No fibrosis</td>
<td></td>
</tr>
<tr>
<td>F1</td>
<td>Portal fibrosis without septa</td>
<td></td>
</tr>
<tr>
<td>F2</td>
<td>Septal fibrosis (portal-portal)</td>
<td></td>
</tr>
</tbody>
</table>
### Cirrhotic Stage of Chronic Liver Disease

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>F3</td>
<td>Septal fibrosis (portal-central)</td>
</tr>
<tr>
<td>F4</td>
<td>Compensated cirrhosis</td>
</tr>
<tr>
<td></td>
<td>Decompensated cirrhosis</td>
</tr>
</tbody>
</table>

### References:


