Protocol for Direct Acting Antiviral Hepatitis C Drugs
Approved June 2016; updated August 2017

Please refer to individual drug PI for specific genotypes and other guidelines.

Preferred agents (See drug-specific note for exceptions):
- For genotype 1, Zepatier is preferred.
- For genotypes 2 and 3, Epclusa is preferred.
- For genotype 4, Zepatier and Epclusa are preferred. (See next note for exceptions.)

Note: Vosevi is intended for retreatment in those who have had a prior trial of antiviral treatment for hepatitis C. It is not intended for treatment naïve individuals. Requests for Vosevi may be approved for individuals with genotypes 1-4 who meet one of the following criteria and Criteria for Approval listed below:
- Individual has had trials and inadequate response to preferred agent(s) of each genotype.
  Or
- Individual is currently completing a course of therapy with requested agent.
  Or
- Individual has documented intolerance to any ingredient in the preferred regimen, which is not part of requested nonpreferred regimen.
  Or
- Individual is concurrently using an agent that cannot be substituted or temporarily discontinued during the course of hepatitis C treatment (for reasons including drug interactions or contraindication to preferred agent).
  Or
- Individual has failed to achieve a sustained virologic response (SVR) or relapsed after achieving a SVR during a prior successfully completed direct-acting antiviral treatment regimen.

Note: Requests for Epclusa® may be approved for individuals with genotype 1 who meet one of the following criteria and Criteria for Approval listed below:
- Individual has had trials and inadequate response to preferred agent(s) of each genotype.
  Or
- Individual is currently completing a course of therapy with requested agent.
  Or
- Individual has documented intolerance to any ingredient in the preferred regimen, which is not part of requested nonpreferred regimen.
  Or
- Individual is concurrently using an agent that cannot be substituted or temporarily discontinued during the course of hepatitis C treatment (for reasons including drug interactions or contraindication to preferred agent).
  Or
- Individual has concomitant moderate or severe hepatic impairment — Child-Turcotte-Pugh (CTP) class B or C.

Note: Requests for Olysio® may be approved for individuals with genotype 1 or 4 who meet one of the following criteria and Criteria for Approval listed below:
- Individual has had trials and inadequate response to preferred agent(s) of each genotype.
  Or
• Individual is currently completing a course of therapy with requested agent.
  Or
• Individual has documented intolerance to any ingredient in the preferred regimen, which is not part of requested nonpreferred regimen.
  Or
• Individual is concurrently using an agent that cannot be substituted or temporarily discontinued during the course of hepatitis C treatment (for reasons including drug interactions or contraindication to preferred agent).

Note: Requests for Mavyret may be approved for individuals with genotype 1, 2, 3 or 4 who meet one of the following criteria and Criteria for Approval listed below:
• Individual has had trials and inadequate response to preferred agent(s) of each genotype.
  Or
• Individual is currently completing a course of therapy with requested agent.
  Or
• Individual has documented intolerance to any ingredient in the preferred regimen, which is not part of requested nonpreferred regimen.
  Or
• Individual is concurrently using an agent that cannot be substituted or temporarily discontinued during the course of Hepatitis C treatment (for reasons including drug interactions or contraindication to preferred agent).

Criteria for Approval:
1. Patient is at least 18 years of age.
   And
2. Patient has diagnosis of chronic hepatitis C; labs showing genotype and detectable HCV RNA levels from within the past 90 days must be received.
   And
3. Patient must have one of the following to be considered at highest risk for hepatitis C-related complications (must receive documentation):
   3.1. Patient has stage 2 fibrosis (METAVIR F2) confirmed by one of the following:
       • Liver biopsy
       • Transient elastography (FibroScan) score greater than or equal to 7.1 kPa
       • FibroTest (FibroSURE) score of greater than or equal to 0.48
       • APRI score greater than 0.7
       • FIB-4 (Fibrosis-4 index) greater than 3.25
       • Radiological imaging consistent with cirrhosis (e.g., evidence of portal hypertension)
   3.2. Patient has type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations (e.g., vasculitis) (AASLD/IDSA 2015).
     Or
   3.3. Patient has nephrotic syndrome or membranoproliferative glomerulonephritis (AASLD/IDSA 2015).
     Or
   3.4. Patient has proteinuria (AASLD/IDSA 2014) as defined by one of the following:
       • One lab result of albumin-to-creatinine ratio (ACR) of greater than 300 mg/g taken within the past 30 days must be received
       • One lab result of ACR of greater than or equal to 30 mg/g taken within the past 30 days must be received AND a second lab result of ACR greater than or equal to 30 mg/g taken within 60 days prior to the most recent test must also be received
3.5. Patient has HIV-1 co-infection (AASLD/IDSA 2015) confirmed by antiretroviral use, on-file diagnosis, or by lab results

And

4. Patient was prescribed by one of the following: hepatologist, gastroenterologist, infectious disease specialist or liver transplant specialist.

And

5. For treatment-experienced patients, must receive medication names and length of therapy, whether patient is a relapsing, null responder, partial responder, or treatment naïve to previous hepatitis C therapy (Provide medication names, dates of fill, length of treatment and HCV RNA levels from the previous therapy.)

6. Patient has evidence of compliance (adherent to therapy) as demonstrated by refill records.

And

7. Initial quantity dispensed will be limited to 14 days dosage units (14-14-28-28 format).

And

8. For patients with severe renal impairment (including CrCl less than 30ml/minute or end-stage renal disease), the urgency to treat must be high and renal transplant must not be an immediate option.

9. Patient must not have any of the following:
   - Contraindications to requested hepatitis C therapy (See PI for complete list.)
   - Patient must not be on any therapies identified by the prescribing information or AASLD/IDSA guidelines as therapies not recommended for co-administration, (see PI and guidelines for complete list)
   - Limited life expectancy (less than 12 months due to nonliver-related comorbidities) — per AASLD guidelines 2015, HCV therapy would not improve symptoms or prognosis in this patient population and do not require treatment.

10. If combined with ribavirin patient will meet all of the following:
    - Patient has no contraindication (See PI for complete list) to ribavirin.
    - Neither the patient nor the partner of the patient is pregnant.
    - If patient or their partner is of childbearing age, the patient has been or will be instructed to practice effective contraception during therapy and for six months after stopping ribavirin therapy.

11. For patients with decompensated cirrhosis, the requested drug(s) must be prescribed by a liver transplant specialist.

### CTP classification for severity of cirrhosis:

<table>
<thead>
<tr>
<th>Clinical and lab criteria</th>
<th>Points</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encephalopathy</td>
<td>None</td>
<td>Grade 1 or 2</td>
<td>Grade 3 or 4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(or precipitant-induced)</td>
<td>(or chronic)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ascites</td>
<td>None</td>
<td>Mild/moderate</td>
<td>Severe</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(diuretic-responsive)</td>
<td>(diuretic-refractory)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilirubin (mg/dL)</td>
<td>&lt; 2</td>
<td>2.3</td>
<td>&gt; 3</td>
<td></td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>&gt; 3.5</td>
<td>2.8-3.5</td>
<td>&lt; 2.8</td>
<td></td>
</tr>
<tr>
<td>Prothrombin time (PT)</td>
<td>&lt;4</td>
<td>4-6</td>
<td>&gt; 6</td>
<td></td>
</tr>
<tr>
<td>Prothrombin time (sec)</td>
<td>&lt;1.7</td>
<td>1.7-2.3</td>
<td>&gt; 2.3</td>
<td></td>
</tr>
<tr>
<td>Prothrombin time (INR)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* CTP class is obtained by adding score for each parameter (total points).

- **Class A** = 5 to 6 points (least severe liver disease)
- **Class B** = 7 to 9 points (moderately severe liver disease)
- **Class C** = 10 to 15 points (most severe liver disease)

From: *Core Concepts. Evaluation and Prognosis of Patients with Cirrhosis* (Karla Thornton, MD, MPH)
Comparison of scoring systems for histological stage (fibrosis):

<table>
<thead>
<tr>
<th>Stage (F)</th>
<th>IASL*</th>
<th>Batt's-Ludwig</th>
<th>Metavir</th>
<th>Ishak</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No fibrosis</td>
<td>No fibrosis</td>
<td>No fibrosis</td>
<td>No fibrosis</td>
</tr>
<tr>
<td>1</td>
<td>Mild fibrosis</td>
<td>Fibrosis portal expansion</td>
<td>Perilobular fibrotic expansion</td>
<td>Fibrosis expansion of some portal areas with or without short fibrous septa</td>
</tr>
<tr>
<td>2</td>
<td>Moderate fibrosis</td>
<td>Rare bridges or septae</td>
<td>Portal fibrosis 1 (septum)</td>
<td>Fibrosis expansion of most portal areas with or without short fibrous septa</td>
</tr>
<tr>
<td>3</td>
<td>Severe fibrosis</td>
<td>Numerous bridges or septae</td>
<td>Portal-central septae</td>
<td>Fibrosis expansion of most portal areas with occasional portal to portal bridging</td>
</tr>
<tr>
<td>4</td>
<td>Cirrhosis</td>
<td>Cirrhosis</td>
<td>Cirrhosis</td>
<td>Fibrosis expansion of most portal areas with marked bridging (portal to portal and portal to central)</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td>Marked bridging (portal to portal and portal to central) with occasional nodules (incomplete cirrhosis)</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td>Cirrhosis</td>
</tr>
</tbody>
</table>

*IASL = The International Association for the Study of Liver

References:
American Association for the Study of Liver Diseases (AASLD)/Infectious Disease Society of America (IDSA).


Harvoni® [Prescribing Information]. Gilead Sciences, Foster City, CA 94404; October 2014.
Sovaldi® [Prescribing Information]. Gilead Sciences, Foster City, CA 94404; December 2013.
Viekira Pak® [Prescribing Information]. AbbVie Inc., North Chicago, IL 60064; December 2014.