### Sovaldi (sofosbuvir)

<table>
<thead>
<tr>
<th>Override(s)</th>
<th>Approval Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior Authorization</td>
<td>Based on Genotype, treatment status, cirrhosis status, hepatocellular carcinoma status, interferon/ribavirin eligibility status, or transplant status</td>
</tr>
<tr>
<td>OR</td>
<td>Genotype, treatment status, cirrhosis status, ribavirin eligibility status, or transplant status</td>
</tr>
</tbody>
</table>

#### Medication

<table>
<thead>
<tr>
<th>Sovaldi (sofosbuvir)</th>
<th>Quantity Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 tablet per day</td>
<td></td>
</tr>
</tbody>
</table>

### APPROVAL DURATION

Based on Genotype, treatment status, cirrhosis status, hepatocellular carcinoma status, interferon/ribavirin eligibility status, or transplant status:

<table>
<thead>
<tr>
<th>Genotype and Status type (HCV Mono-infected or HCV/HIV-1 Co-infected)</th>
<th>Associated Treatment Regimens</th>
<th>Total Approval Duration for Sovaldi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype 1 (treatment-naive or -experienced*, post-liver allograft transplant, with or without compensated cirrhosis)</td>
<td>Sovaldi + Olysio ± RBV</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 3 (treatment-naive or -experienced*, post-liver allograft transplant, with or without compensated cirrhosis)</td>
<td>Sovaldi + RBV</td>
<td>24 weeks</td>
</tr>
<tr>
<td>Genotype 3 (post-liver allograft transplant, with decompensated cirrhosis)</td>
<td>Sovaldi + RBV</td>
<td>24 weeks</td>
</tr>
<tr>
<td>Genotype 1 (with or without compensated cirrhosis)</td>
<td>Sovaldi + IFN + RBV</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 1 (treatment-naive or dual treatment-experienced*, without compensated cirrhosis)</td>
<td>Sovaldi + Olysio</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 1a (treatment-naive or dual treatment-experienced*, with compensated cirrhosis, without Q80K polymorphism)</td>
<td>Sovaldi + Olysio ± RBV</td>
<td>24 weeks</td>
</tr>
<tr>
<td>Genotype 1b (treatment-naive, or dual treatment-experienced* with compensated cirrhosis)</td>
<td>Sovaldi + Olysio ± RBV</td>
<td>24 weeks</td>
</tr>
<tr>
<td>Genotype 1 (treatment-naive, with or without compensated cirrhosis, interferon ineligible)</td>
<td>Sovaldi + RBV</td>
<td>24 weeks</td>
</tr>
<tr>
<td>Genotype 2 (dual treatment-experienced***, with or without compensated cirrhosis, interferon eligible)</td>
<td>Sovaldi + IFN + RBV</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 2 (treatment-naive, with or without compensated cirrhosis)</td>
<td>Sovaldi + RBV</td>
<td>12 weeks^</td>
</tr>
</tbody>
</table>
**Genotype 2 (dual treatment-experienced\(^\dagger\), with or without compensated cirrhosis)**  
Sovaldi + RBV  
16 weeks\(^\wedge\)

**Genotype 3 (treatment-naïve or dual treatment-experienced\(^\dagger\), with or without compensated cirrhosis)**  
Sovaldi + RBV  
24 weeks

**Genotype 3 (treatment naïve or dual treatment-experienced\(^\ast\) with or without compensated cirrhosis, interferon eligible)**  
Sovaldi + IFN + RBV  
12 weeks

**Genotype 4 (treatment-naïve or dual treatment-experienced\(^\ast\), with or without compensated cirrhosis, interferon eligible)**  
Sovaldi + IFN + RBV  
12 weeks

**Genotype 4 (treatment-naïve or dual treatment-experienced\(^\ast\), with or without compensated cirrhosis)**  
Sovaldi + RBV  
24 weeks

**Genotype 5 or 6 (treatment-naïve, with or without compensated cirrhosis)**  
Sovaldi + IFN + RBV  
12 weeks

**Hepatocellular Carcinoma awaiting liver transplant**  
Sovaldi + RBV  
Up to 48 weeks**

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\(^{a}\)Per the AASLD/IDSA 2015, support for Sovaldi and Olysio combination use in the liver post-transplant population is based on ongoing prospective studies in treatment-naïve and -experienced patients. Studies conducted in the treatment-experienced population mostly comprise prior regimens of interferon and ribavirin or interferon, ribavirin, and Incivek or Victrelis.

\(^{b}\)A clinical trial completed with sofosbuvir and ribavirin following liver transplant recipients defines treatment-experienced in these specific populations as a prior failed trial of interferon and ribavirin; sofosbuvir and ribavirin; or interferon, ribavirin, and a HCV protease inhibitor (Incivek, Victrelis, or Olysio).

\(^{c}\)Per Olysio label, treatment-experienced includes prior dual therapy (interferon and ribavirin) relapsers (HCV RNA not detected at the end of prior IFN-based therapy and detected during follow-up), prior partial responders (prior on-treatment ≥ 2 log\(_{10}\) IU/mL reduction in HCV RNA from baseline at Week 12 and HCV RNA detected at end of prior dual therapy) or prior null responders (prior on-treatment < 2 log\(_{10}\) reduction in HCV RNA from baseline at Week 12 during prior dual therapy).

\(^{d}\)Dual treatment-experienced refers to individuals who have had a partial response, no response, or prior relapse with a previous dual therapy regimen of interferon and ribavirin.

\(^{\wedge}\)Therapy duration may be extended up to 8 additional weeks for a total of 24 weeks (AASLD/IDSA 2014).

**Based on Genotype, treatment status, cirrhosis status, ribavirin eligibility status, or transplant status**

<table>
<thead>
<tr>
<th>Genotype and Status (HCV mono-infected or HCV/HIV-1 co-infected(^a))</th>
<th>Associated Treatment Regimens</th>
<th>Total Approval Duration for Sovaldi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype 1 (treatment-naïve or -experienced, without compensated cirrhosis)</td>
<td>Sovaldi + Daklinza</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 1 (treatment-naïve or -experienced, with compensated cirrhosis)</td>
<td>Sovaldi + Daklinza ± RBV</td>
<td>24 weeks</td>
</tr>
<tr>
<td>Genotype 2 (treatment-naïve, without compensated cirrhosis, ribavirin ineligible/intolerant)</td>
<td>Sovaldi + Daklinza</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 2 (treatment-naïve, with compensated cirrhosis, ribavirin ineligible/intolerant)</td>
<td>Sovaldi + Daklinza</td>
<td>24 weeks</td>
</tr>
<tr>
<td>Genotypes 1, 2, 3, or 4 (treatment-naïve or -experienced(^d), post-liver allograft transplant, with or without compensated cirrhosis)</td>
<td>Sovaldi + Daklinza + RBV</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotypes 1, 2, 3, or 4 (treatment-naïve or -experienced(^d) with decompenesated cirrhosis)</td>
<td>Sovaldi + Daklinza + RBV</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 3 (treatment-naïve or dual treatment-experienced(^\ast), with compensated cirrhosis)</td>
<td>Sovaldi + Daklinza + RBV</td>
<td>24 weeks</td>
</tr>
<tr>
<td>Genotype 3 (treatment-naïve or dual treatment-experienced(^\ast), without compensated cirrhosis)</td>
<td>Sovaldi + Daklinza</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>
The August 2015 AASLD/IDSA treatment guidance update references clinical trials that define treatment-experienced in these specific populations as a prior failed trial of interferon and ribavirin or a HCV protease inhibitor (Incivek, Victrelis, or Olysio), interferon, and ribavirin.

The August 2015 AASLD/IDSA treatment guidance update references clinical trials that define treatment-experienced in these specific populations as a prior failed trial of interferon and ribavirin; sofosbuvir and ribavirin; or interferon, ribavirin, and a HCV protease inhibitor (Incivek, Victrelis, or Olysio).

Daklinza clinical trials conducted in these specific populations defined dual treatment-experienced as a prior trial with interferon ± ribavirin or sofosbuvir and ribavirin.

**APPROVAL CRITERIA**

Requests for Sovaldi (sofosbuvir) may be approved if the following criteria are met:

I. Individual is 18 years of age or older; **AND**

II. A copy of the baseline quantitative hepatitis C virus (HCV) RNA test result is provided to document baseline level of viremia; **AND**

III. Documentation is provided for a diagnosis of chronic hepatitis C (CHC) infection, which includes genotype\(^a\) and a persistent positive HCV RNA test result for at least 6 months following positive baseline result (AASLD/IDSA 2015); **AND**

IV. Individual does not have a short life expectancy (less than 12 months owing to non-liver related comorbid conditions) that cannot be remediated by treating HCV, by transplantation or other directed therapy (AASLD/IDSA 2015); **AND**

V. Individual has one of the following:

   a. Genotypes 1, 2, 3, 4, 5, or 6 and compensated liver disease\(^1\) (with or without cirrhosis; Label, AASLD/IDSA 2015); **OR**

   b. Genotypes 1, 2, 3, or 4 and decompensated\(^1\) liver disease (with cirrhosis, AASLD/IDSA 2015);

**AND**

VI. Individual meets one of the following:

   a. Individual is not actively abusing illicit drugs and/or alcohol; **OR**

   b. Individual is receiving concurrent treatment to facilitate cessation of drug and/or alcohol abuse (AASLD/IDSA 2015);

**AND**

VII. Individual is using with one of the following antiviral treatment regimens:

   a. In combination with peg interferon and ribavirin for one of the following:

      1. Individuals with or without compensated\(^1\) cirrhosis, Genotype 1, and has had a trial of Harvoni; **OR**

      2. Individual is dual (interferon and ribavirin) treatment-experienced with or without compensated\(^1\) cirrhosis, eligible for interferon, and Genotype 2 (AASLD/IDSA 2015); **OR**

      3. Individual is treatment naïve or dual (interferon and ribavirin) treatment-experienced with or without compensated\(^1\) cirrhosis, eligible for interferon, and Genotype 3 (AASLD/IDSA 2015); **OR**

      4. Individual is treatment-naïve or dual (interferon and ribavirin) treatment-experienced (AASLD/IDSA 2015) with or without compensated\(^1\) cirrhosis, eligible for interferon, Genotype 4, and has had a trial of Harvoni; **OR**

      5. Individual is treatment-naïve with or without compensated\(^1\) cirrhosis and Genotypes 5 or 6 (AASLD/IDSA 2015); **OR**
b. In combination with ribavirin alone for **one** of the following:
   1. Individual is treatment-naïve with or without compensated cirrhosis, Genotype 1, a trial of Harvoni is clinically inappropriate (for example but not limited to, hypersensitivity), and is ineligible for an interferon-based regimen, as defined by the presence of **one** of the following:
      i. Intolerance to interferon (AASLD/IDSA 2015); **OR**
      ii. Autoimmune disorders (AASLD/IDSA 2015), including autoimmune hepatitis; **OR**
      iii. Child-Pugh score greater than 6 (Class B or C)\(^1\) before or during interferon treatment; **OR**
      iv. Known hypersensitivity to interferon products; **OR**
      v. History of uncontrolled major depression, clinical features consistent with depression, or suicidal ideation (AASLD 2009, AASLD/IDSA 2015); **OR**
      vi. Uncontrolled epilepsy (EASL 2015); **OR**
      vii. Retinal disease (EASL 2015); **OR**
      viii. Baseline neutrophil count below 1500/µL, baseline platelet count below 90,000/µL or baseline hemoglobin below 10 g/dL (AASLD/IDSA 2015); **OR**
      ix. History of preexisting cardiac disease (AASLD/IDSA 2015);

   **OR**
   2. Individual is treatment-naïve or dual (interferon and ribavirin) treatment-experienced with or without compensated\(^1\) cirrhosis and Genotype 2; **OR**
   3. Individual is treatment-naïve or dual (interferon and ribavirin) treatment-experienced with or without compensated\(^1\) cirrhosis and Genotype 3; **OR**
   4. Individual is treatment-naïve or -experienced (interferon and ribavirin or interferon, ribavirin and a HCV protease inhibitor), post-liver allograft transplant, with or without compensated\(^1\) cirrhosis and Genotype 3 (AASLD/IDSA 2015, Charlton et al. 2015); **OR**
   5. Individual is post-liver allograft transplant with decompensated\(^1\) cirrhosis and Genotype 3 (AASLD/IDSA 2015); **OR**
   6. Individual is treatment naïve or dual (interferon and ribavirin) treatment-experienced with or without compensated\(^1\) cirrhosis, Genotype 4 (AASLD/IDSA 2015), and has had a trial of Harvoni; **OR**
   7. Individuals with CHC and concurrent hepatocellular carcinoma meeting Milan criteria\(^b\) (awaiting liver transplantation);

   **OR**
   c. In combination with Olysio (simeprevir) in individuals without compensated\(^1\) cirrhosis and Genotype 1 who meet the following:
      1. Individual has had a trial of Harvoni: **AND**
      2. Individual is treatment-naïve or dual (interferon and ribavirin) treatment-experienced.

   **OR**
   d. In combination with Olysio (simeprevir) with or without ribavirin for the following:
      1. Individual has had a trial of Harvoni; **AND**
      2. Individual meets the following:
i. Individuals with Genotype 1a or 1b with compensated\textsuperscript{1} cirrhosis; \textbf{AND}

ii. Individual is treatment-naïve or dual (interferon and ribavirin) treatment-experienced; \textbf{AND}

iii. Individual has been screened and is negative for the NS3Q80K polymorphism associated with HCV Genotype 1a subtype (AASLD/IDSA 2015);

\textbf{OR}

iv. Individual is treatment-naïve or -experienced (interferon and ribavirin or interferon, ribavirin, and Incivek or Victrelis), post-liver allograft transplant recipient with or without compensated\textsuperscript{1} cirrhosis, and Genotype 1 (AASLD/IDSA 2015);

\textbf{OR}

e. In combination with Daklinza (daclatasvir) for one of the following:

1. Individual is treatment-naïve or -experienced (interferon and ribavirin or interferon, ribavirin and a HCV protease inhibitor) without compensated\textsuperscript{1} cirrhosis, Genotype 1 (AASLD/IDSA 2015) and has had a trial of Harvoni; \textbf{OR}

2. Individual is treatment-naïve with or without compensated\textsuperscript{1} cirrhosis, ribavirin ineligible/intolerant (such as but not limited to, pregnant women, hemoglobinopathies), and Genotype 2 (AASLD/IDSA 2015); \textbf{OR}

3. Individual is treatment-naïve or dual (interferon ± ribavirin or sofosbuvir + ribavirin) treatment-experienced without compensated\textsuperscript{1} cirrhosis and Genotype 3 (Daklinza label);

\textbf{OR}

f. In combination with Daklinza (daclatasvir) with or without ribavirin (AASLD/IDSA 2015); \textbf{AND}

g. Individual is treatment-naïve or treatment-experienced (interferon and ribavirin or interferon, ribavirin, and a HCV protease inhibitor) with compensated\textsuperscript{1} cirrhosis, Genotype 1, and has had a trial of Harvoni;

\textbf{OR}

h. In combination with Daklinza (daclatasvir) and ribavirin for one of the following (AASLD/IDSA 2015):

1. Individual is treatment-naïve or -experienced (interferon and ribavirin; or interferon, ribavirin, and a HCV protease inhibitor), post-liver allograft transplant with or without compensated\textsuperscript{1} cirrhosis, Genotypes 1 or 4, and has had a trial of Harvoni; \textbf{OR}

2. Individual is treatment-naïve or -experienced (sofosbuvir and ribavirin), post-liver allograft transplant with or without compensated\textsuperscript{1} cirrhosis and Genotypes 1 or 4; \textbf{OR}

3. Individual is treatment-naïve or -experienced (interferon and ribavirin; sofosbuvir and ribavirin; or interferon, ribavirin, and a HCV protease inhibitor), post-liver allograft transplant with or without compensated\textsuperscript{1} cirrhosis and Genotypes 2 or 3; \textbf{OR}
4. Individual is treatment-naïve or -experienced (interferon and ribavirin; sofosbuvir and ribavirin; or interferon, ribavirin, and a HCV protease inhibitor) with decompensated\(^1\) cirrhosis, Genotypes 1 or 4; OR

5. Individual is treatment-naïve or -experienced (interferon and ribavirin; sofosbuvir and ribavirin; or interferon, ribavirin, and a HCV protease inhibitor) with decompensated\(^1\) cirrhosis and Genotypes 2 or 3; OR

6. Individual is treatment-naïve or dual (interferon ± ribavirin or sofosbuvir + ribavirin) treatment-experienced with compensated\(^1\) cirrhosis and Genotype 3.

Sovaldi (sofosbuvir) may **not** be approved for the following:

I. Individual has severe renal impairment (CrCl less than 30 mL/min), end stage renal disease, or requires dialysis OR

II. Individual is requesting in concurrent therapy with contraindicated or not recommended agents, such as but not limited to the following: amiodarone, carbamazepine, phenytoin, phenobarbital, oxcarbazepine, rifabutin, rifampin, rifapentine, St John’s Wort, or tipranavir/ritonavir; OR

III. Individual is using in combination with a non-nucleoside NS5B polymerase inhibitor (such as but not limited to dasabuvir) or another nucleotide NS5B polymerase inhibitor (such as Harvoni [sofosbuvir/ledipasvir]); OR

IV. Individual is using in combination with a NS3/4A protease inhibitor other than Olysio (simeprevir) [such as but not limited to Incivek (telaprevir), Victrelis (boceprevir), or paritaprevir]; OR

V. Individual is using in combination with a NS5A inhibitor other than ledipasvir or Daklinza (daclatasvir) (such as but not limited to, ombitasvir); OR

VI. Individual is requesting for re-treatment in combination with Olysio (simeprevir) and either failed to achieve a SVR (defined as a lower limit HCV RNA of 25 IU/mL) or relapsed after achieving a SVR during a prior successfully completed treatment regimen consisting of a serine NS3/4A protease inhibitor (simeprevir, paritaprevir, or asunaprevir); OR

VII. Individual is requesting for re-treatment in combination with Olysio (simeprevir) and either failed to achieve a SVR (defined as a lower limit HCV RNA of 25 IU/mL) or relapsed after achieving a SVR during a prior successfully completed treatment regimen consisting of telaprevir or boceprevir, unless requested following post-liver allograft transplant); OR

VIII. Individual is requesting re-treatment in combination with Olysio (simeprevir) and either failed to achieve an SVR (defined as a lower limit HCV RNA of 25 IU/mL) or relapsed after achieving an SVR during a prior successfully completed treatment regimen consisting of sofosbuvir (such as Harvoni); OR

IX. Individual is requesting for re-treatment in combination with Daklinza (daclatasvir) and either failed to achieve a SVR (defined as a lower limit HCV RNA of 25 IU/mL) or relapsed after achieving a SVR during a prior successfully completed treatment regimen consisting of a NS5A inhibitor [such as but not limited to, Daklinza (daclatasvir), ledipasvir, or ombitasvir] (AASLD/IDSA 2015); OR

X. Individual is requesting for re-treatment in combination with Daklinza (daclatasvir) and either failed to achieve a SVR (defined as a lower limit HCV RNA of 25 IU/mL) or relapsed after achieving a SVR during a prior successfully completed treatment regimen consisting of paritaprevir (AASLD/IDSA 2015); OR
XI. Individual is requesting the regimen for re-treatment in combination with Daklinza (daclatasvir) and either failed to achieve a SVR (defined as a lower limit HCV RNA of 25 IU/mL) or relapsed after achieving a SVR during a prior successfully completed treatment regimen consisting of sofosbuvir, ribavirin, and interferon; OR

XII. Individual is requesting in combination with ribavirin or interferon and ribavirin and has received previous treatment for hepatitis C virus (HCV) with one of the following:
   a. An interferon-based triple therapy regimen, which includes ribavirin and a serine NS3/4A inhibitor [Incivek (telaprevir), Victrelis (boceprevir), or Olysio (simeprevir)], unless sofosbuvir and ribavirin are being requested following post-liver allograft transplant; OR
   b. An interferon-based triple therapy regimen, which includes ribavirin and Sovaldi (sofosbuvir); OR
   c. A therapy regimen containing a NS5A inhibitor [such as but not limited to, Harvoni (ledipasvir/sofosbuvir), Daklinza (daclatasvir), or ombitasvir]; OR
   d. A therapy regimen containing a serine NS3/4A protease inhibitor [such as but not limited to, Incivek (telaprevir), Victrelis (boceprevir), Olysio (simeprevir), paritaprevir, or asunaprevir]; OR
   e. A therapy regimen containing a NS5B polymerase inhibitor [such as but not limited to, Sovaldi (sofosbuvir), Harvoni (ledipasvir/sofosbuvir), or dasabuvir].

*Notes:

a Per label and AASLD/IDSA 2015 treatment guidance, Sovaldi (sofosbuvir) may be used in individuals co-infected with human immunodeficiency virus (HIV)-1 either in combination with interferon and ribavirin (label), ribavirin (label), Olysio (simeprevir) (AASLD/IDSA 2015), or Daklinza (daclatasvir) (AASLD/IDSA 2015). Concurrent use of Sovaldi with all antiretroviral therapy is allowable with the exception of tipranavir/ritonavir.

b Milan criteria: A solitary tumor less than or equal to 5 cm or up to three (3) nodules less than or equal to 3 cm each with no extrahepatic manifestations or evidence of vascular invasion of tumor.

1. **Compensated Liver Disease:**
According to the American Association for the Study of Liver Diseases (AASLD, 2009, 2015), the specific criteria for compensated liver disease include all of the following: a total bilirubin; serum albumin; prothrombin time/INR; presence of ascites; and presence of hepatic encephalopathy. However, these criteria do not establish a comprehensive definition of compensated liver disease. The AASLD guidance refers to compensated liver disease as Class A based on the Child Pugh-Turcotte (CPT) classification scoring system.

**Child Pugh Classification (AASLD/IDSA 2015)**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>1 point</th>
<th>2 points</th>
<th>3 points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Bilirubin (µmol/L)</td>
<td>&lt;34</td>
<td>34-50</td>
<td>&gt;50</td>
</tr>
<tr>
<td>Serum Albumin (g/L)</td>
<td>&gt;35</td>
<td>28-35</td>
<td>&lt;28</td>
</tr>
<tr>
<td>Prothrombin time/INR</td>
<td>&lt;1.7</td>
<td>1.71-2.30</td>
<td>&gt;2.30</td>
</tr>
<tr>
<td>Ascites</td>
<td>None</td>
<td>Mild</td>
<td>Moderate to Severe</td>
</tr>
<tr>
<td>Hepatic Encephalopathy</td>
<td>None</td>
<td>Grade I-II (or suppressed with medication)</td>
<td>Grade III-IV (or refractory)</td>
</tr>
</tbody>
</table>
**Child Pugh Score Interpretation (AASLD/IDSA 2009, 2015)**

<table>
<thead>
<tr>
<th>Class</th>
<th>Score Range</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>5-6 points</td>
<td>Well compensated liver disease</td>
</tr>
<tr>
<td>B</td>
<td>7-9 points</td>
<td>Significant functional compromise (moderate hepatic impairment)</td>
</tr>
<tr>
<td>C</td>
<td>10-15 points</td>
<td>Uncompensated liver disease (severe hepatic impairment)</td>
</tr>
</tbody>
</table>

**2. Scoring Systems for Fibrosis Staging (AASLD 2009):**

<table>
<thead>
<tr>
<th>Stage (F)</th>
<th>IASL*</th>
<th>Batt-Ludwig</th>
<th>Metavir</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</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>Periportal fibrotic expansion</td>
</tr>
<tr>
<td>2</td>
<td>Moderate fibrosis</td>
<td>Rare bridges or septae</td>
<td>Periportal septae 1 (septum)</td>
</tr>
<tr>
<td>3</td>
<td>Severe fibrosis</td>
<td>Numerous bridges or septae</td>
<td>Porto-central septae</td>
</tr>
<tr>
<td>4</td>
<td>Cirrhosis</td>
<td>Cirrhosis</td>
<td>Cirrhosis</td>
</tr>
</tbody>
</table>

*IASL = The International Association for the Study of Liver

<table>
<thead>
<tr>
<th>Stage (F)</th>
<th>Ishak</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No fibrosis</td>
</tr>
<tr>
<td>1</td>
<td>Fibrosis expansion of some portal areas with or without short fibrous septa</td>
</tr>
<tr>
<td>2</td>
<td>Fibrous expansion of most portal areas with or without short fibrous septa</td>
</tr>
<tr>
<td>3</td>
<td>Fibrous expansion of most portal areas with occasional portal to portal bridging</td>
</tr>
<tr>
<td>4</td>
<td>Fibrous expansion of most portal areas with marked bridging (portal to portal and portal to central)</td>
</tr>
<tr>
<td>5</td>
<td>Marked bridging (portal to portal and portal to central) with occasional nodules (incomplete cirrhosis)</td>
</tr>
<tr>
<td>6</td>
<td>Cirrhosis</td>
</tr>
</tbody>
</table>

**State Specific Mandates**

| N/A | N/A | N/A |

**Key References:**


