1. **Background:**

Harvoni™ (ledipasvir/sofosbuvir) is a fixed-dose combination of ledipasvir, a hepatitis C virus (HCV) NS5A inhibitor, and sofosbuvir, an HCV nucleotide analog NS5B polymerase inhibitor, and is indicated for the treatment of chronic hepatitis C (CHC) genotype 1, 4, 5, or 6 infection in adults.¹

2. **Coverage Criteria:**

A. For the treatment of chronic hepatitis C genotype 1 infection in treatment-naïve patients without cirrhosis who have pre-treatment HCV RNA less than 6 million IU/mL, Harvoni will be approved based on all of the following criteria:

1. Submission of medical records (e.g., chart notes, laboratory values) documenting diagnosis of chronic hepatitis C genotype 1 infection

   -AND-

2. Submission of medical records documenting stage of liver disease (eg, APRI score, FibroSure score, Fibroscan score, or other methods)

   -AND-

3. Patient is treatment-naïve [patient has not experienced treatment failure (defined as viral relapse, breakthrough while on therapy, or nonresponder to therapy) with peginterferon plus ribavirin or peginterferon plus ribavirin plus an HCV protease inhibitor (e.g., Incivek, Olysio, Victrelis) or Sovaldi (sofosbuvir)]

   -AND-

4. Submission of laboratory report documenting a pre-treatment HCV RNA less than 6 million IU/mL

   -AND-

5. Prescribed by one of the following:
   
   a. Hepatologist
   b. Gastroenterologist
   c. Infectious Disease Specialist
   d. HIV Specialist Certified through the Academy of HIV Medicine
6. One of the following:
   a. Patient has no known history of illicit drug abuse or alcohol abuse

   -OR-

   b. For a patient with a known prior history of illicit drug abuse or alcohol abuse:
      
      (1) Patient has abstained from the use of illicit drugs and alcohol abuse for the past 6 months

   -AND-

      (2) For a patient with a prior history of illicit drug abuse, submission of a negative urine drug screen collected within 30 days prior to onset of treatment**

   -AND-

7. Patient is not receiving Harvoni in combination with another HCV direct acting antiviral agent [e.g., Sovaldi (sofosbuvir), Olysio (simeprevir)]

**Authorization will be issued for 8 weeks.

B. For the treatment of chronic hepatitis C genotype 1 infection in treatment-naïve patients without cirrhosis who have pre-treatment HCV RNA equal to or greater than 6 million IU/mL OR Post Transplant OR on immunosuppressants OR co-infected with HIV, Harvoni will be approved based on all of the following criteria:

1. Submission of medical records (e.g., chart notes, laboratory values) documenting diagnosis of chronic hepatitis C genotype 1 infection

   -AND-

2. Submission of medical records documenting stage of liver disease (eg, APRI score, FibroSure score, Fibroscan score, or other methods)

   -AND-

3. Patient is treatment-naïve [patient has not experienced treatment failure (defined as viral relapse, breakthrough while on therapy, or nonresponder to therapy) with peginterferon plus ribavirin or peginterferon plus ribavirin plus an HCV protease inhibitor (eg, Incivek, Olysio, Victrelis) or Sovaldi (sofosbuvir)]

   -AND-
4. **One** of the following:
   a. Submission of laboratory report documenting a pre-treatment HCV RNA equal to or greater than 6 million IU/mL
   -**OR**-
   b. Patient is taking immunosuppressant therapy following organ transplantation or for another condition
   -**OR**-
   c. Patient is co-infected with HIV
   -**AND**-

5. Prescribed by **one** of the following:
   a. Hepatologist
   b. Gastroenterologist
   c. Infectious Disease Specialist
   d. HIV Specialist Certified through the Academy of HIV Medicine
   -**AND**-

6. **One** of the following:
   a. Patient has no known history of illicit drug abuse or alcohol abuse
   -**OR**-
   b. For a patient with a known prior history of illicit drug abuse or alcohol abuse:
      (1) Patient has abstained from the use of illicit drugs and alcohol abuse for the past 6 months
      -**AND**-
      (2) For a patient with a prior history of illicit drug abuse, submission of a negative urine drug screen collected within 30 days prior to onset of treatment**
      -**AND**-

7. Patient is not receiving Harvoni in combination with another HCV direct acting antiviral agent [e.g., Sovaldi (sofosbuvir), Olysio (simeprevir)]

**Authorization will be issued for 12 weeks.**
C. For the treatment of chronic hepatitis C genotype 1 infection in treatment-naïve patients with cirrhosis, Harvoni will be approved based on all of the following criteria:

1. Submission of medical records (e.g., chart notes, laboratory values) documenting diagnosis of chronic hepatitis C genotype 1 infection
   -AND-

2. Submission of medical records (eg, chart notes, laboratory values) documenting that the patient has cirrhosis
   -AND-

3. Patient is treatment-naïve [patient has not experienced treatment failure (defined as viral relapse, breakthrough while on therapy, or nonresponder to therapy) with peginterferon plus ribavirin or peginterferon plus ribavirin plus an HCV protease inhibitor (e.g., Incivek, Olysio, Victrelis) or Sovaldi (sofosbuvir)]
   -AND-

4. Prescribed by one of the following:
   a. Hepatologist
   b. Gastroenterologist
   c. Infectious Disease Specialist
   d. HIV Specialist Certified through the Academy of HIV Medicine
   -AND-

5. One of the following:
   a. Patient has no known history of illicit drug abuse or alcohol abuse
   -OR-

   b. For a patient with a known prior history of illicit drug abuse or alcohol abuse:
      (1) Patient has abstained from the use of illicit drugs and alcohol abuse for the past 6 months
      -AND-

      (2) For a patient with a prior history of illicit drug abuse, submission of a negative urine drug screen collected within 30 days prior to onset of treatment**
      -AND-

6. Patient is not receiving Harvoni in combination with another HCV direct acting antiviral
agent [eg, Sovaldi (sofosbuvir), Olysio (simeprevir)]

Authorization will be issued for 12 weeks.

D. For the treatment of chronic hepatitis C genotype 1 infection in treatment-experienced patients without cirrhosis, Harvoni will be approved based on all of the following criteria:

1. Submission of medical records (e.g., chart notes, laboratory values) documenting diagnosis of chronic hepatitis C genotype 1 infection

   -AND-

2. Submission of medical records documenting stage of liver disease (eg, APRI score, FibroSure score, Fibroscan score, or other methods)

   -AND-

3. Prescribed by one of the following:
   a. Hepatologist
   b. Gastroenterologist
   c. Infectious Disease Specialist
   d. HIV Specialist Certified through the Academy of HIV Medicine

   -AND-

4. One of the following:
   a. Patient has no known history of illicit drug abuse or alcohol abuse

   -OR-

   b. For a patient with a known prior history of illicit drug abuse or alcohol abuse:

      (1) Patient has abstained from the use of illicit drugs and alcohol abuse for the past 6 months

      -AND-

      (2) For a patient with a prior history of illicit drug abuse, submission of a negative urine drug screen collected within 30 days prior to onset of treatment **

      -AND-

5. Patient has experienced treatment failure, defined as viral relapse/breakthrough while on therapy or non-responder to therapy, with a previous treatment regimen that included peginterferon plus ribavirin or an HCV protease inhibitor (e.g. Incivek, Olysio,
Vicarelis) plus peginterferon plus ribavirin or Sovaldi (sofosbuvir)

-AND-

6. Patient is not receiving Harvoni in combination with another HCV direct acting antiviral agent [e.g., Sovaldi (sofosbuvir), Olysio (simeprevir)]

Authorization will be issued for 12 weeks.

E. For the treatment of chronic hepatitis C genotype 1 infection in treatment-experienced patients with cirrhosis, Harvoni will be approved based on all of the following criteria:

1. Submission of medical records (e.g., chart notes, laboratory values) documenting diagnosis of chronic hepatitis C genotype 1 infection assessment, liver biopsy)

-AND-

2. Submission of medical records (e.g., chart notes, laboratory values) documenting that the patient has cirrhosis

-AND-

3. Prescribed by one of the following:
   a. Hepatologist
   b. Gastroenterologist
   c. Infectious Disease Specialist
   d. HIV Specialist Certified through the Academy of HIV Medicine

-AND-

4. One of the following:
   a. Patient has no known history of illicit drug abuse or alcohol abuse

-OR-

b. For a patient with a known prior history of illicit drug abuse or alcohol abuse:
   (1) Patient has abstained from the use of illicit drugs and alcohol abuse for the past 6 months

-AND-

(2) For a patient with a prior history of illicit drug abuse, submission of a negative urine drug screen collected within 30 days prior to onset of treatment**
5. Patient has experienced treatment failure, defined as viral relapse/breakthrough while on therapy or non-responder to therapy, with a previous treatment regimen that included peginterferon plus ribavirin or an HCV protease inhibitor (e.g. Incivek, Olysio, Victrelis) plus peginterferon plus ribavirin or Sovaldi (sofosbuvir)

-AND-

6. Patient is not receiving Harvoni in combination with another HCV direct acting antiviral agent [e.g., Sovaldi (sofosbuvir), Olysio (simeprevir)]

**Authorization will be issued for 24 weeks.**

F. For the treatment of chronic hepatitis C genotype 4, 5 or 6 infection, Harvoni will be approved based on all of the following criteria:

1. Submission of medical records (e.g., chart notes, laboratory values) documenting diagnosis of chronic hepatitis C genotype 4, 5 or 6 infection

-AND-

2. Submission of medical records documenting stage of liver disease (eg, APRI score, FibroSure score, Fibroscan score, or other methods)

-AND-

3. Prescribed by one of the following:
   a. Hepatologist
   b. Gastroenterologist
   c. Infectious Disease Specialist
   d. HIV Specialist Certified through the Academy of HIV Medicine

-AND-

4. One of the following:
   a. Patient has no known history of illicit drug abuse or alcohol abuse

   -OR-

   b. For a patient with a known prior history of illicit drug abuse or alcohol abuse:
      (1) Patient has abstained from the use of illicit drugs and alcohol abuse for the past 6 months
For a patient with a prior history of illicit drug abuse, submission of a negative urine drug screen collected within 30 days prior to onset of treatment**

5. Patient is not receiving Harvoni in combination with another HCV direct acting antiviral agent [e.g., Sovaldi (sofosbuvir), Olysio (simeprevir)]

Authorization will be issued for 12 weeks.

*Comparison of Scoring Systems for Histological Stage (Fibrosis)*

<table>
<thead>
<tr>
<th>METAVIR</th>
<th>Batts-Ludwig</th>
<th>Knodell</th>
<th>Ishak</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>--</td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

**Positive urine drug screen findings will not necessarily disqualify the member for authorization if they can be explained by the finding of a legitimate prescription for medication that would result in a positive test (i.e., methylphenidate causing positive findings for amphetamines, hydrocodone causing positive findings for opiates, etc.). A urine drug screen testing positive for cannabinoids will not disqualify authorization if there is a contemporaneous prescription for Marinol, or if the physician attests to prescribing medical marijuana in states where legal, or in states where the recreational use of marijuana has been legalized.

3. Additional Clinical Rules:

Supply Limits may be in place.

4. References:


<table>
<thead>
<tr>
<th>Program</th>
<th>Prior Authorization/Medical Necessity - Harvoni (ledipasvir/sofosbuvir)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change Control</td>
<td></td>
</tr>
<tr>
<td>8/2015</td>
<td>Added criteria for genotype 4 infection</td>
</tr>
<tr>
<td>11/2015</td>
<td>Changed program title to include all lines of business, added genotypes 5 and 6, and updated language regarding documentation of liver fibrosis.</td>
</tr>
</tbody>
</table>