



UnitedHealthcare Pharmacy  
Clinical Pharmacy Programs

Program Number	2014 P 2043-1
Program	Prior Authorization/Medical Necessity
Medication	Harvoni™ (ledipasvir/sofosbuvir)
P&T Approval Date	10/2014
Effective Date	10/15/2014

**1. Background:**

The standard of care for the treatment of hepatitis C infection is rapidly evolving due to the entry of highly effective direct-acting oral antiviral agents which are expected to be approved by the US Food and Drug Administration (FDA) over the next 2 years. The first evolution in the treatment of hepatitis C occurred in May 2011 when the standard of care for the treatment of hepatitis C genotype 1 infection shifted to the use of triple therapy with the introduction of first-generation oral NS3/4A protease inhibitors which significantly improved viral cure rates from 44% to 72% when added to the previous standard of care of pegylated interferon and ribavirin combination therapy. In December 2013 another shift occurred in the treatment paradigm which for the first time included highly effective, all oral, interferon-free regimens for the treatment of genotypes 2 and 3 hepatitis C infection, as well as providing the improvement of shorter-duration triple therapy with new oral direct acting agents combined with pegylated interferon and ribavirin for the treatment of genotypes 1 and 4 hepatitis C infection. With this latest shift in treatment, the first-generation protease inhibitors, Victrelis® (boceprevir) and Incivek® (telaprevir), are no longer recommended as standard of care for the treatment of hepatitis C genotype 1 infection.

UnitedHealthcare's coverage criteria for the new direct-acting agents are based on careful consideration of the evidence-based guidance of professional specialty societies, published guidelines and physician subject matter experts. The Infectious Diseases Society of America (IDSA) and American Association for the Study of Liver Diseases (AASLD) have jointly published evidence-based, expert-developed recommendations for hepatitis C which stated the following about prioritization of treatment with direct acting agents: " Treatment is assigned the highest priority for those patients with advanced fibrosis (Metavir F3), those with compensated cirrhosis (Metavir F4), liver transplant recipients, and patients with severe extrahepatic hepatitis C. Based on available resources, treatment should be prioritized as necessary so that patients at high risk for liver-related complications and severe extrahepatic hepatitis C complications are given high priority ." <sup>1</sup> In addition, a report issued in February 2014 by the Institute for Clinical and Economic Review (ICER) for the California Technology Assessment Forum (CTAF) recommended that Olysio and Sovaldi be used only for patients with severe hepatitis complications, such as liver cirrhosis. <sup>2</sup>

As part of our commitment to provide affordable health care benefits, UnitedHealthcare actively monitors the development of new clinical evidence and availability of new products and may adjust coverage and strategy accordingly. Based on current evidenced-based guidance from professional specialty societies and physician subject matter experts, UnitedHealthcare will provide benefit coverage in cases of hepatitis C infection when there is documented evidence of stage 3 or stage 4 hepatic fibrosis.

## 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. **Both** of the following:

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

**-AND-**

b. **One** of the following:

(1) Submission of medical records (e.g., chart notes, laboratory values) documenting stage 3 hepatic fibrosis including **one** of the following:

(a) Liver biopsy confirming a METAVIR score of F3, or alternative scoring equivalent\*

**-OR-**

(b) Transient elastography (Fibroscan) score greater than or equal to 9.5 kPa

**-OR-**

(c) FibroTest (FibroSURE) score of greater than or equal to 0.58

**-OR-**

(d) APRI score greater than 1.5

**-OR-**

(2) Submission of medical records (e.g., chart notes, laboratory values) documenting that patient has serious extrahepatic manifestations of HCV infection (i.e., leukocytoclastic vasculitis, membranoproliferative glomerulonephritis, or symptomatic cryoglobulinemia)

**-OR-**

(3) Patient is co-infected with HIV

**-AND-**

2. 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-**

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

**-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\*\*

**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-Liver Transplant, **Harvoni** will be approved based on **all** of the following criteria:

1. **Both** of the following:
  - a. Submission of medical records (e.g., chart notes, laboratory values) documenting diagnosis of chronic hepatitis C genotype 1 infection

**-AND-**

b. **One** of the following:

(1) Submission of medical records (e.g., chart notes, laboratory values) documenting stage 3 hepatic fibrosis including **one** of the following:

(a) Liver biopsy confirming a METAVIR score of F3, or alternative scoring equivalent\*

**-OR-**

(b) Transient elastography (Fibroscan) score greater than or equal to 9.5 kPa

**-OR-**

(c) FibroTest (FibroSURE) score of greater than or equal to 0.58

**-OR-**

(d) APRI score greater than 1.5

**-OR-**

(2) Submission of medical records (e.g., chart notes, laboratory values) documenting genotype 1 HCV reinfection following liver transplantation

**-OR-**

(3) Submission of medical records (e.g., chart notes, laboratory values) documenting that patient has serious extrahepatic manifestations of HCV infection (i.e., leukocytoclastic vasculitis, membranoproliferative glomerulonephritis, or symptomatic cryoglobulinemia)

**-OR-**

(4) Patient is co-infected with HIV

**-AND-**

2. 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-**

3. **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 has genotype 1 HCV reinfection following liver transplantation

**-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\*\*

**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. **Both** of the following:

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

**-AND-**

b. **One** of the following:

(1) Submission of medical records (e.g., chart notes, laboratory values) documenting stage 4 hepatic fibrosis including **one** of the following:

(a) Liver biopsy confirming a METAVIR score of F4, or alternative scoring equivalent\*

**-OR-**

(b) Transient elastography (Fibroscan) score greater than or equal to 12.5 kPa

**-OR-**

(c) FibroTest (FibroSURE) score of greater than or equal to 0.75

**-OR-**

(d) APRI score greater than 2.0

**-OR-**

(e) Radiological imaging consistent with cirrhosis (e.g., evidence of portal hypertension)

**-OR-**

(f) Physical findings or clinical evidence consistent with cirrhosis as attested by the prescribing physician

**-AND-**

2. Patient is treatment-naive [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-**

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\*\*

**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. **Both** of the following:

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

**-AND-**

b. **One** of the following:

- (1) Submission of medical records (e.g., chart notes, laboratory values) documenting stage 3 hepatic fibrosis including **one** of the following:

- (a) Liver biopsy confirming a METAVIR score of F3, or alternative scoring equivalent\*

**-OR-**

- (b) Transient elastography (Fibroscan) score greater than or equal to 9.5 kPa

**-OR-**

- (c) FibroTest (FibroSURE) score of greater than or equal to 0.58

**-OR-**

(d) APRI score greater than 1.5

**-OR-**

(2) Submission of medical records (e.g., chart notes, laboratory values) documenting genotype 1HCV reinfection following liver transplantation

**-OR-**

(3) Submission of medical records (e.g., chart notes, laboratory values) documenting that patient has serious extrahepatic manifestations of HCV infection (i.e., leukocytoclastic vasculitis, membranoproliferative glomerulonephritis, or symptomatic cryoglobulinemia)

**-OR-**

(4) Patient is co-infected with HIV

**-AND-**

2. 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-**

3. **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-**

4. 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)

**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. **Both** of the following:

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

**-AND-**

b. Submission of medical records (e.g., chart notes, laboratory values) documenting stage 4 hepatic fibrosis including **one** of the following:

(1) Liver biopsy confirming a METAVIR score of F4, or alternative scoring equivalent\*

**-OR-**

(2) Transient elastography (Fibroscan) score greater than or equal to 12.5 kPa

**-OR-**

(3) FibroTest (FibroSURE) score of greater than or equal to 0.75

**-OR-**

(4) APRI score greater than 2.0

**-OR-**

(5) Radiological imaging consistent with cirrhosis (e.g., evidence of portal hypertension)

**-OR-**

(6) Physical findings or clinical evidence consistent with cirrhosis as attested by the prescribing physician

**-AND-**

2. 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-**

3. **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-**

- 4. 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)

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

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

METAVIR	Batts-Ludwig	Knodell	Ishak
0	0	0	0
1	1	1	1
1	1	1	2
2	2	--	3
3	3	3	4
4	4	4	5
4	4	4	6

\*\*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:**

1. American Association for the Study of Liver Diseases and the Infectious Diseases Society of America. Recommendations for When and In Whom to Initiate HCV Therapy. August 2014. <http://www.hcvguidelines.org/full-report-view>. Accessed October 13, 2014.
2. California Technology Assessment Forum. The Comparative Clinical Effectiveness and Value of Simeprevir and Sofosbuvir in the Treatment of Chronic Hepatitis C Infection. <http://www.ctaf.org/reports/treatments-hepatitis-c> Accessed October 13, 2014.
3. Harvoni [package insert]. Foster City, CA: Gilead Sciences, Inc.; October 2014.

Program	Prior Authorization/Medical Necessity - Harvoni (ledipasvir/sofosbuvir)
<b>Change Control</b>	
10/2014	New program.