VENTURA COUNTY
HEALTH CARE PLAN

Prior Authorization DRUG Guidelines

HARVONI (ledipasvir and sofosbuvir)

Effective Date: 1/1/16
Date Developed: 12/31/15 by Catherine R. Sanders, MD and Robert Sterling, MD
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Harvoni is a combination of ledipasvir which inhibits the HCV NS5A protein necessary for viral replication and sofosbuvir, a prodrug converted to its pharmacologically active form (GS-461203), inhibits NS5B RNA-dependent RNA polymerase, also essential for viral replication, and acts as a chain terminator.

Pre-Authorization Criteria:
Harvoni may be authorized for the treatment of Chronic Hepatitis C when patients meet the following criteria:

1. **Chronic Hepatitis C (HCV) Genotype 1.** Approve Harvoni for the specified duration below if patients meet all of the following criteria (A, B, C, and D):
   - **A)** The patient is ≥ 18 years of age; AND
   - **B)** Harvoni is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician; AND
   - **C)** **According to the prescribing physician** the patient meets ONE of the following conditions (i, ii, or iii):
     - **i.** The patient has been documented as having a hepatic fibrosis score correlating with **Metavir Stage ≥F2** as assessed by an invasive (liver biopsy) OR non-invasive method (e.g., aspartate aminotransferase-to-platelet ratio index [APRI] score, fibrosis-4 index [FIB-4], FibroScan, FibroTest/FibroSURE); OR
     - **ii.** The patient has **severe extrahepatic manifestations** placing them at high risk for severe complications of their HCV (patient must meet criteria 1 or 2):
       - **(1)** Type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations (e.g., vasculitis); OR
       - **(2)** Proteinuria, nephrotic syndrome, or membranoproliferative glomerular nephritis; OR
     - **iii.** The patient meets BOTH of the following conditions (1 and 2):
       - **(1)** The patient is at **high-risk of transmitting HCV** (patient must meet ONE of the following criteria a or b):
         - **a.** The patient is on long-term (≥ 3 months) hemodialysis; OR
         - **b.** The patient is a healthcare worker whose daily activities put them in contact with blood and/or needles; AND
       - **(2)** The patient has been counseled on ways to decrease transmission of HCV and minimize the risk of reinfection with HCV; AND
   - **D)** The patient meets ONE of the following criteria (i, ii or iii):
     - **i.** **Approve for 8 weeks** in patients who meet all of the following (1, 2 and 3):
       - **(1)** The patient is treatment-naïve; AND

(2) The patient does not have cirrhosis; AND

(3) The patient does not have human immunodeficiency virus (HIV) (patients with HIV should be reviewed the same as patients without HIV using *Criteria ii or iii below*); AND

(4) The patient is not awaiting liver transplantation (patients awaiting liver transplantation should be reviewed using *Criteria ii or iii below*) AND

(5) Baseline HCV RNA is < 6 million IU/mL. OR

ii. **Approve for 12 weeks** in patients who meet one the following (1 or 2):

(1) The patient is treatment-naïve AND does not meet criterion D) i above (this would include patients with or without HIV who are treatment-naïve with compensated (Child-Pugh A) cirrhosis regardless of baseline HCV RNA, or treatment-naïve patients with or without HIV without cirrhosis and baseline HCV RNA ≥ 6 million IU/mL. This would also include treatment-naïve patients awaiting transplant with compensated cirrhosis [Child-Pugh A] regardless of baseline HCV RNA, or treatment-naïve patients awaiting transplant without cirrhosis and baseline HCV RNA ≥ 6 million IU/mL); OR

(2) The patient has previously been treated for HCV and does not have cirrhosis (for patients with compensated cirrhosis (Child-Pugh A) see *iii below, for patients with decompensated cirrhosis (Child-Pugh B or C) see (3) below*); OR

(3) The patient is treatment-naïve or has previously been treated for hepatitis C virus (HCV) and meets both of the following criteria (a) and (b):
(a) The patient has decompensated (Child-Pugh B or C) cirrhosis; AND
(b) Harvoni will be prescribed in combination with ribavirin. OR

iii. **Approve for 24 weeks** if the patient has previously been treated for hepatitis C virus (HCV) and has compensated (Child-Pugh A) cirrhosis.

2. Chronic Hepatitis C Virus (HCV) – Genotype 4, 5 OR 6. Approve Harvoni for 12 weeks in patients who meet the above criteria (1 A, B and C):

3. Recurrent Hepatitis C Virus (HCV) Post-Liver Transplantation, Genotypes 1 and 4. Approve for the specified duration in patients who meet the following criteria (A, B, C and D):

A) The patient is ≥ 18 years of age; AND

B) The patient has recurrent hepatitis C virus (HCV) after a liver transplantation; AND

C) Harvoni is prescribed by or in consultation with one of the following prescribers who is affiliated with a transplant center[2]: a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician; AND

D) The patient meets ONE of the following criteria (i or ii):

i. **Approve for 12 weeks** in patients who meet one of the following criteria (a or b):

a) The patient is treatment-naïve *for recurrent hepatitis C virus (HCV)*; OR

b) The patient has previously been treated *for recurrent hepatitis C virus (HCV)* AND does not have cirrhosis; OR

ii. **Approve for 24 weeks** in patients who have previously been treated *for recurrent HCV* and have cirrhosis.

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Exceptions: Harvoni is not to be approved for patients with a life expectancy less than 12 months due to non-liver related comorbidities. Harvoni is not be approved for patients who have previously received Harvoni. Harvoni is not to be used in combination with any other direct-acting antivirals

Medication Guide or Rx restrictions:

Dosing:
Chronic hepatitis C (CHC) infection in monoinfected (HCV) or coinfected (HCV/HIV-1) genotype 1 patients: Oral: Treatment regimen and duration based on clinical scenario as noted below; fixed-dose tablet is ledipasvir 90 mg and sofosbuvir 400 mg:
Treatment-naive patients with or without cirrhosis or treatment-experienced patients without cirrhosis: One tablet once daily for 12 weeks.
Treatment-experienced patients with cirrhosis:
Used without concomitant ribavirin: One tablet once daily for 24 weeks.
Used with concomitant ribavirin in eligible patients: One tablet daily with concomitant ribavirin for 12 weeks.
Note: Treatment-naive patients without cirrhosis who have HCV RNA <6 million units/mL may be considered for therapy of 8 weeks duration. Treatment-experienced patients are defined as those in whom treatment has failed with a peginterferon alfa plus ribavirin based regimen with or without an HCV protease inhibitor.
Chronic hepatitis C (CHC) infection in monoinfected (HCV) or coinfected (HCV/HIV-1) genotype 4, 5 or 6 patients: Oral: Treatment regimen and duration based on clinical scenario as noted below; fixed-dose tablet is ledipasvir 90 mg and sofosbuvir 400 mg:
Treatment-naive patients with or without cirrhosis or treatment-experienced patients with or without cirrhosis: One tablet once daily for 12 weeks.
Note: Treatment-experienced patients are defined as those in whom treatment has failed with a peginterferon alfa plus ribavirin based regimen with or without an HCV protease inhibitor.

Dosing Forms:
Harvoni: Ledipasvir 90 mg and sofosbuvir 400 mg

Major Adverse reactions:
Fatigue, headache, insomnia, nausea, diarrhea, increased serum lipase, hyperbilirubinemia.

Warnings:
Symptomatic bradycardia has been reported with Harvoni in combination with amiodarone, or Sovaldi in combination with amiodarone and another direct-acting antiviral (eg simeprevir). Administration of amiodarone with Harvoni or Sovaldi is not recommended.

References:
-Department of Health Care Services, Treatment Policy for the Management of Chronic Hepatitis C, July 1, 2015.
-UpToDate Drug Information Ledipasvir and sofosbuvir, 2016.

-American Association of the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA), "Recommendations for Testing, Managing, and Treating Hepatitis C" found at http://www.hcvguidelines.org/full-report-view.
-Afdhal N, Zeuzem S, KWO P, et al; ION-1 Investigators. Ledipasvir and sofosbuvir for untreated HCV genotype 1 infection. *N Engl J Med*. 2014;370(20):1889-1898. [PubMed 24725239]

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