PRIOR AUTHORIZATION POLICY

POLICY: Hepatitis C – Harvoni Prior Authorization Policy
- Harvoni® (ledipasvir/sofosbuvir tablets and oral pellets – Gilead)
- ledipasvir/sofosbuvir tablets (authorized generic to Harvoni 90 mg/400 mg tablets– Asegua)

REVIEW DATE: 09/11/2024

INSTRUCTIONS FOR USE

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CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

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. It is indicated for the treatment of **chronic HCV** infection in patients ≥ 3 years of age in the following instances:[1]
- Genotype 1, 4, 5, or 6 infections with or without compensated cirrhosis; and
- Genotype 1 infection with decompensated cirrhosis, in combination with ribavirin; and
- Genotype 1 or 4 infection who are liver transplant recipients with or without compensated cirrhosis, in combination with ribavirin.

Dosing

In adults, the recommended dose of ledipasvir/sofosbuvir is one tablet taken orally once daily with or without food.[1] The recommended dose of ledipasvir/sofosbuvir tablets or pellets in pediatric patients ≥ 3 years of age is based on weight. The ledipasvir/sofosbuvir pellets can be taken in pediatric patients who cannot swallow the tablet formulation. Table 1 below provides the recommended duration of therapy with ledipasvir/sofosbuvir. The ledipasvir/sofosbuvir authorized generic is only available in the 90 mg/400 mg strength tablet; Harvoni is additionally available as a lower strength tablet (45 mg/200 mg) as well as oral pellets (45 mg/200 mg and 33.75 mg/150 mg).

Table 1. Recommended Treatment Duration for ledipasvir/sofosbuvir in Patients ≥ 3 Years of Age with Chronic HCV Genotype 1, 4, 5, or 6.[1]

Patient Population	Duration of Treatment
Genotype 1 – Treatment-naïve with or without compensated (Child Pugh A) cirrhosis	ledipasvir/sofosbuvir 12 weeks*
Genotype 1 – Treatment-experienced** without cirrhosis	ledipasvir/sofosbuvir 12 weeks
Genotype 1 – Treatment-experienced** with compensated (Child Pugh A) cirrhosis	ledipasvir/sofosbuvir 24 weeks†
Genotype 1 – Treatment-naïve and treatment-experienced** with decompensated (Child-Pugh B or C) cirrhosis.	ledipasvir/sofosbuvir + ribavirin‡ 12 weeks
Genotype 1 or 4 – Transplant recipients without cirrhosis, or with compensated (Child-Pugh A) cirrhosis	ledipasvir/sofosbuvir + ribavirin§ 12 weeks
Genotype 4, 5, or 6 – Treatment-naïve and treatment-experienced**, with or without compensated (Child-Pugh A) cirrhosis	ledipasvir/sofosbuvir12 weeks

HCV – Hepatitis C virus; * Harvoni for 8 weeks can be considered in treatment-naïve patients without cirrhosis who have pretreatment HCV RNA < 6 million IU/mL; ** Treatment-experienced patients who have failed treatment with either peginterferon alfa + ribavirin or a hepatitis C virus protease inhibitor + peginterferon + ribavirin; † Harvoni for 12 weeks can be considered in treatment-experienced patients with cirrhosis who are eligible for ribavirin. The daily dose of ribavirin is weight-based (1,000 mg for patients < 75 kg and 1,200 mg for those ≥ 75 kg) administered in two divided doses. ‡ In patients with decompensated cirrhosis, the starting dosage of ribavirin is 600 mg and can be titrated up to 1,000 mg for patients < 75 kg and 1,200 mg for those ≥ 75 kg in two divided doses with food. If the starting dosage of ribavirin is not well tolerated, the dosage should be reduced as clinically indicated based on hemoglobin levels. § The daily dosage of ribavirin is weight-based (1,000 mg for patients < 75 kg and 1,200 mg for those ≥ 75 kg) administered orally in two divided doses with food.

Guidelines

The American Association for the Study of Liver Diseases/Infectious Diseases Society of America have simplified recommendations for the management of chronic HCV in adults (December 19, 2023).[2] In treatment-naïve adults without cirrhosis, the recommended regimens are Mavyret® (glecaprevir/pibrentasvir tablets and oral pellets) for 8 weeks or Epclusa® (sofosbuvir/velpatasvir tablets [generic] and oral pellets) for 12 weeks. In treatment-naïve adults with compensated cirrhosis, the recommended regimens are Mavyret for 8 weeks (genotypes 1 through 6) or sofosbuvir/velpatasvir for 12 weeks (genotypes 1, 2, 4, 5, or 6; patients with genotype 3 require baseline NS5A resistance-associated substitution testing and those without Y93H can be treated with 12 weeks of Epclusa). Additional genotype-specific and/or special circumstance-specific recommendations are also provided for patients falling outside of these parameters.

Ledipasvir/sofosbuvir continues to be recommended in various situations as outlined below in Table 2.

Table 2. AASLD Recommendations for Harvoni.[2]

DAA	Duration	FDA Approved (Y/N)	AASLD Level of Evidence
Genotype 1, 4, 5, and 6 Chronic HCV Treatment-Naïve Adults – Recommended			
ledipasvir/sofosbuvir	12 weeks (± compensated cirrhosis) Not recommended for genotype 6e if subtype is known.	Y	Class I, Level A Class IIa, Level B (Genotype 4 compensated cirrhosis, Genotype 5/6 ± compensated cirrhosis)
ledipasvir/sofosbuvir	8 weeks (HIV-uninfected, HCV RNA < 6 million IU/mL, no cirrhosis, absence of genotype 4r)	Y	Class I, Level B
Genotype 1, 4, 5, or 6 Chronic HCV, Decompensated Cirrhosis Adults Ribavirin Eligible – Recommended			
ledipasvir/sofosbuvir + ribavirin	12 weeks	Y	Class I, Level A
Genotype 1, 4, 5, or 6 Chronic HCV, Decompensated Cirrhosis Adults Ribavirin Ineligible – Recommended			
ledipasvir/sofosbuvir	24 weeks	N	Class I, Level A
Genotype 1, 4, 5, or 6 Chronic HCV, Decompensated Cirrhosis Adults Prior Sovaldi or NSA Failure – Recommended			
ledipasvir/sofosbuvir + ribavirin	24 weeks	N	Class II, Level C
Genotype 1, 4, 5, or 6 Recurrent HCV Post-Liver Transplant, No Cirrhosis, Treatment-Naïve or Treatment-Experienced – Recommended			
ledipasvir/sofosbuvir	12 weeks	Y	Class I, Level B
Genotype 1, 4, 5, or 6 Recurrent HCV Post-Liver Transplant, Compensated Cirrhosis, Treatment-Naïve or Treatment-Experienced – Recommended			
ledipasvir/sofosbuvir	12 weeks	Y	Class I, Level A
Genotype 1, 4, 5, or 6 Recurrent HCV Post-Liver Transplant, Decompensated Cirrhosis, Treatment-Naïve or Treatment-Experienced – Recommended			
ledipasvir/sofosbuvir + ribavirin	12 to 24 weeks	Y	Class I, Level B
Genotype 1, 4, 5, or 6 Kidney Transplant Treatment-Naïve or DAA-Experienced ± Compensated Cirrhosis, Adults – Recommended			
ledipasvir/sofosbuvir	12 weeks	N	Class I, Level A
Genotype 1, 4, 5, or 6 Treatment-Naïve Adolescents ≥ 3 years, ± Compensated Cirrhosis – Recommended			
ledipasvir/sofosbuvir	12 weeks	Y	Class I, Level B

Table 2 (continued). AASLD Recommendations for Harvoni.[2]

DAA	Duration	FDA Approved (Y/N)	AASLD Level of Evidence
Genotype 1, 4, 5, or 6 Treatment-Experienced (Interferon + Protease Inhibitor) Adolescents ≥ 3 years, ± Compensated Cirrhosis – Recommended			
ledipasvir/sofosbuvir	12 weeks (genotype 1 no cirrhosis)	Y	Class I, Level C

ledipasvir/sofosbuvir	24 weeks (genotype 1 compensated cirrhosis)	Y	Class I, Level C
ledipasvir/sofosbuvir	12 weeks (genotypes 4, 5, or 6 ± compensated cirrhosis)	Y	Class I, Level C

AASLD – American Association for the Study of Liver Diseases; DAA – Direct-acting antiviral; Y – Yes; N – No; HCV – Hepatitis C virus; HIV – Human immunodeficiency virus.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of ledipasvir/sofosbuvir. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with ledipasvir/sofosbuvir as well as the monitoring required for adverse events and long-term efficacy, approval requires ledipasvir/sofosbuvir to be prescribed by or in consultation with a physician who specializes in the condition being treated.

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is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indications

1. **Chronic Hepatitis C Virus (HCV), Genotype 1.** Approve for the duration noted if the patient meets ALL of the following (A, B, and C):
   - **A)** Patient is ≥ 3 years of age; AND
   - **B)** Patient meets ONE of the following (i, ii or iii):
     - **i.** Approve for 8 weeks if the patient meets ALL of the following (a, b, c, d, and e):
       - **a)** Patient is treatment-naïve; AND
       - **b)** Patient does not have cirrhosis; AND
       - **c)** Patient does not have human immunodeficiency virus (HIV); AND
         Note: Patients with HIV should be reviewed using the same criteria as patients without HIV, using *Criteria ii or iii below*.
       - **d)** Patient is not awaiting liver transplantation; AND
         Note: Patients awaiting liver transplantation should be reviewed using *Criteria ii or iii below.*
       - **e)** Baseline HCV RNA is < 6 million IU/mL; OR
     - **ii.** Approve for 12 weeks if the patient meets ONE the following (a, b, or c):
       - **a)** Patient is treatment-naïve AND does not meet criterion *Bi* above; OR
         Note: Treatment-naïve includes 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 [Child-Pugh A] cirrhosis regardless of baseline HCV RNA or treatment-naïve patients awaiting transplant without cirrhosis and baseline HCV RNA ≥ 6 million IU/mL).
       - **b)** Patient has previously been treated for HCV and does not have cirrhosis; OR

Note: For patients with compensated cirrhosis [Child-Pugh A] see criterion *Biii* below, for patients with decompensated cirrhosis [Child-Pugh B or C] see criterion *Biic* below.

c) Patient is treatment-naïve or has previously been treated for HCV and meets ALL of the following [(1), (2), and (3)]:
(1) Patient has decompensated (Child-Pugh B or C) cirrhosis; AND
(2) Patient is ribavirin eligible; AND
Note: For ribavirin ineligible patients with decompensated cirrhosis, see criterion *Biiib* below.
(3) The medication will be prescribed in combination with ribavirin; OR

iii. Approve for 24 weeks if the patient meets ONE of the following (a or b):
a) Patient has previously been treated for HCV and has compensated (Child-Pugh A) cirrhosis; OR
b) Patient is treatment-naïve or has previously been treated for HCV and the patient meets BOTH of the following [(1) and (2)]:
(1) Patient has decompensated cirrhosis (Child-Pugh B or C); AND
(2) Patient is ribavirin ineligible, according to the prescriber; AND

C) The medication is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician.

2. Chronic Hepatitis C Virus (HCV), Genotypes 4, 5, OR 6. Approve for 12 weeks if the patient meets BOTH of the following (A and B):
A) Patient is ≥ 3 years of age; AND
B) The medication is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician.

3. Recurrent Hepatitis C Virus (HCV) Post-Liver Transplantation, Genotypes 1 OR 4. Approve for 12 weeks if the patient meets ALL of the following (A, B, C and D):
A) Patient is ≥ 3 years of age; AND
B) Patient has recurrent HCV after a liver transplantation; AND
C) The medication will be prescribed in combination with ribavirin; AND
D) The medication is prescribed by or in consultation with one of the following prescribers who is affiliated with a transplant center: a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician.

Other Uses with Supportive Evidence

4. Recurrent Hepatitis C Virus (HCV) Post-Liver Transplantation, Genotypes 5 OR 6. Approve for 12 weeks if the patient meets ALL of the following (A, B, C and D):
A) Patient is ≥ 18 years of age; AND
B) Patient has recurrent HCV after a liver transplantation; AND
C) The medication will be prescribed in combination with ribavirin; AND
D) The medication is prescribed by or in consultation with one of the following prescribers who is affiliated with a transplant center: a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician.

5. Hepatitis C Virus (HCV) in Kidney Transplant Recipients, Genotypes 1 or 4. Approve for 12 weeks if the patient meets ALL of the following (A, B, and C):
A) Patient is ≥ 18 years of age; AND
B) Patient is a kidney transplant recipient with HCV; AND
C) The medication is prescribed by or in consultation with one of the following prescribers who is affiliated with a transplant center: a gastroenterologist,

hepatologist, infectious diseases physician, nephrologist, liver transplant physician, or a renal transplant physician.

6. **Patient Has Been Started on ledipasvir/sofosbuvir.** Approve ledipasvir/sofosbuvir for an indication or condition addressed as an approval in the Recommended Authorization Criteria section (FDA-Approved Indications or Other Uses with Supportive Evidence). Approve for the duration described above to complete a course of therapy (e.g., a patient who should receive 12 weeks and has received 3 weeks, should be approved for 9 weeks to complete their 12-week course).

CONDITIONS NOT COVERED

- **Harvoni® (ledipasvir/sofosbuvir tablets and oral pellets (Gilead)**
- **ledipasvir/sofosbuvir tablets (authorized generic to Harvoni 90 mg/400 mg tablets– Asegua)**

is(are) considered experimental, investigational, or unproven for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Hepatitis C Virus (HCV) [any genotype], Combination with Any Other Direct-Acting Antivirals (DAAs) Not Including Ribavirin.** Ledipasvir/sofosbuvir provides a complete antiviral regimen. Ledipasvir/sofosbuvir is not recommended to be used with other products containing sofosbuvir.

2. **Pediatric Patient (Age < 3 years).** The safety and efficacy of ledipasvir/sofosbuvir have not been established in pediatric patients < 3 years of age.[1]

3. **Retreatment with ledipasvir/sofosbuvir in Patients Who Have Previously Received ledipasvir/sofosbuvir (e.g., retreatment in prior null responders, prior partial responders, prior relapse patients, patients who have not completed a course of therapy due to an adverse reaction or for other reasons)**. There are other direct-acting antivirals indicated for patients who have previously been treated with ledipasvir/sofosbuvir.

REFERENCES

1. Harvoni® tablets and oral pellets [prescribing information]. Foster City, CA: Gilead; March 2020.
2. American Association for the Study of Liver Diseases and the Infectious Diseases Society of America. Testing, managing, and treating hepatitis C. Available at: http://www.hcvguidelines.org. Updated December 19, 2023. Accessed on August 19, 2024.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	09/13/2023
Selected Revision	**Conditions Not Covered : Life Expectancy Less Than 12 Months Due to Non-Liver Related Comorbidities**. This condition was removed.	02/28/2024

Annual Revision	No criteria changes.	09/11/2024