Drug Coverage Policy

Effective Date……07/01/2025
Coverage Policy Number……IP0735
Policy Title…..Harvoni Prior Authorization 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)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support

medical necessity and other coverage determinations.

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 infection 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

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.

Coverage Policy

POLICY STATEMENT

Prior Authorization is required for prescription benefit coverage of ledipasvir/sofosbuvir products. 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.

NOTE: This product also requires the use of preferred products before approval of the requested product. Refer to the *Hepatitis C Virus Direct-Acting Antivirals Preferred Specialty Management Policy for Employer Plans (PSM025)* for additional preferred product criteria requirements and exceptions.

Ledipasvir/sofosbuvir products are considered medically necessary when ONE of the following is met (1, 2, 3, 4, 5, or 6):

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 above criteria sections (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).

Ledipasvir/sofosbuvir products for any other use is considered not medically necessary, 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.

Revision Details

Type of Revision	Summary of Changes	Date
New	New policy	07/01/2025

The policy effective date is in force until updated or retired.