Drug Quantity Management – Per Days
Hepatitis C – Harvoni

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Product Identifier(s)

Effective 1/1/23 to 2/6/23: 107992

Effective 2/7/23: 47992

INSTRUCTIONS FOR USE
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National Formulary Medical Necessity

Drugs Affected

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

This Drug Quantity Management program has been developed to prevent to prevent stockpiling, misuse and/or overuse of ledipasvir/sofosbuvir (Harvoni, generic). If the Drug Quantity Management rule is not met for the requested medication at the point of service, coverage will be determined by the Criteria below. All approvals are provided for 1 year in duration unless otherwise noted below.

Drug Quantity Limits

Product	Strength and Form	Maximum Quantity per 365 days
Harvoni®	90/400 mg tablet	56 tablets (28 tablets/28 days)
	45/200 mg tablet	112 tablets (56 tablets/28 days)
(ledipasvir/sofosbuvir)	45/200 mg pellet packet	112 packets (56 packets/28 days)
	33.75/150 mg pellet packet	56 packets (28 packets/28 days)
Ledipasvir/sofosbuvir (authorized generic)	90/400 mg tablet	56 tablets (28 tablets/28 days)

Note: Individuals can fill 28 tablets or packets/28 days, to the maximum quantity per 365 days or 56 tablets or packets/28 days to the maximum quantity per 365 days depending on the dosage form outlined in the table.

Criteria

Cigna covers quantities as medically necessary when the following criteria are met:

Ledipasvir/sofosbuvir 90 mg/400 mg tablets (Harvoni, generic)

1. **Chronic Hepatitis C Virus, Genotype 1.**
   - **A)** Approve 84 tablets per 365 days at retail or home delivery if the individual meets ONE of the following (i, ii, or iii):
     - **i.** Individual is treatment-naïve AND meets at least ONE of the following (a, b, or c):
       - **a)** Individual has compensated cirrhosis (Child-Pugh A) [includes individuals awaiting liver transplant]; OR
       - **b)** Individual does not have cirrhosis and baseline HCV RNA ≥ 6 million IU/mL (includes individuals awaiting liver transplant); OR
       - **c)** Individual has human immunodeficiency virus.
     - **ii.** Individual has previously been treated for HCV and does not have cirrhosis; OR
     - **iii.** Individual is treatment-naïve OR has previously been treated for HCV AND meets both of the following criteria (a and b):
       - **a)** Individual has decompensated cirrhosis (Child-Pugh B or C); AND
       - **b)** The medication will be prescribed in combination with ribavirin.

     Note: This is a quantity sufficient to treat with one tablet per day for 12 weeks.
   - **B)** Approve 168 tablets per 365 days at retail or home delivery if the individual meets ONE of the following (i or ii):
     - **i.** Individual has previously been treated for HCV AND has compensated cirrhosis (Child-Pugh A); OR
     - **ii.** Individual is treatment-naïve OR has previously been treated for HCV AND meets both of the following criteria (a and b):
       - **a)** Individual has decompensated cirrhosis (Child-Pugh B or C); AND
       - **b)** Individual is ribavirin ineligible, according to the prescriber.

     Note: This is a quantity sufficient to treat with one tablet per day for 24 weeks.

2. **Chronic Hepatitis C Virus, Genotype 4, 5, or 6.** Approve 84 tablets per 365 days at retail or home delivery.
   Note: This is a quantity sufficient to treat with one tablet per day for 12 weeks.

3. **Recurrent Hepatitis C Virus Post-Liver Transplantation, Genotype 1, 4, 5, OR 6.** Approve 84 tablets per 365 days at retail or home delivery.
   Note: This is a quantity sufficient to treat with one tablet per day for 12 weeks.

4. **Hepatitis C Virus Kidney Transplant Recipient, Genotype 1 or 4.** Approve 84 tablets per 365 days at retail or home delivery.
   Note: This is a quantity sufficient to treat with one tablet per day for 12 weeks.

5. For an indication or condition addressed as an approval in the above criteria section, approve the quantity requested, not to exceed 168 tablets per 365 days at retail or home delivery, to complete a course therapy.

Note: For example, if the individual has received 4 weeks of therapy (28 tablets) and is eligible for 12 weeks of treatment, approve 56 tablets to complete 12 weeks of therapy. If an individual has received 4 weeks (28 tablets) of therapy and is eligible for 24 weeks of treatment, approve 140 tablets to complete 24 weeks of therapy.

Harvoni 45 mg/200 mg tablets, Harvoni 45 mg/200 mg pellet packets

1. **Chronic Hepatitis C Virus (HCV) Genotype 1.**
   - **A)** Approve 168 tablets or pellet packets per 365 days at retail or home delivery if the individual meets criterion (i) AND meets ONE of the following (ii or iii or iv):
     - **i.** Individual is < 12 years of age; AND
     - **ii.** Individual is treatment-naïve AND meets at least ONE of the following (a, b, or c):
       - **a)** Individual has compensated cirrhosis (Child-Pugh A) [includes individuals awaiting liver transplant]; OR
       - **b)** Individual does not have cirrhosis and baseline HCV RNA ≥ 6 million IU/mL (includes individuals awaiting liver transplant); OR
       - **c)** Individual has human immunodeficiency virus. OR
     - **iii.** Individual has previously been treated for HCV and does not have cirrhosis; OR
     - **iv.** Individual is treatment-naïve OR has previously been treated for HCV AND meets both of the following criteria (a and b):
       - **a)** Individual has decompensated cirrhosis (Child-Pugh B or C); AND
       - **b)** The medication will be prescribed in combination with ribavirin.

     Note: This is a quantity sufficient for two tablets or two pellet packets per day for 12 weeks.
   - **B)** Approve 336 tablets or pellet packets per 365 days at retail or home delivery if the individual meets BOTH of the following criteria (i and ii):
     - **i.** Individual is < 12 years of age; AND
     - **ii.** Individual meets ONE of the following (a or b):
       - **a)** Individual has previously been treated for HCV AND has compensated cirrhosis (Child-Pugh A); OR
       - **b)** Individual is treatment-naïve OR has previously been treated for HCV AND meets both of the following criteria (1 and 2):
         - **(1)** Individual has decompensated cirrhosis (Child-Pugh B or C);
         - **(2)** Individual is ribavirin ineligible, according to the prescriber.

     Note: This is a quantity sufficient for two tablets or two pellet packets per day for 24 weeks.

2. **Chronic Hepatitis C Virus Genotype, 4, 5, or 6.** If the individual is < 12 years of age, approve 168 tablets or pellet packets per 365 days at retail or home delivery.
   Note: This is a quantity sufficient to treat with two tablets or pellet packets per day for 12 weeks.

3. **Recurrent Hepatitis C Virus Post-Liver Transplantation, Genotype 1 OR 4.** If the individual is < 12 years of age**,** approve 168 tablets or pellet packets per 365 days at retail or home delivery.
   Note: This is a quantity sufficient to treat with two tablets or pellet packets per day for 12 weeks.

4. For an indication or condition addressed as an approval in the above criteria section, approve the quantity requested, not to exceed 336 tablets or pellet packets per 365 days at retail or home delivery, to complete a course therapy.
   Note: For example, if the individual has received 4 weeks of therapy (56 tablets or pellet packets) and is eligible for 12 weeks of treatment, approve 112 tablets to complete 12 weeks of therapy. If an individual has received 4 weeks (56 tablets or pellet packets) of therapy and is eligible for 24 weeks of treatment, approve 280 tablets or pellet packets to complete 24 weeks of therapy.

Harvoni 33.75 mg/150 mg pellet packets

1. **Chronic Hepatitis C Virus Genotype 1**.
   - **A)** Approve 84 pellet packets per 365 days at retail or home delivery if the individual meets BOTH of the following (i and ii):
     - **i.** Individual is < 12 years of age; AND
     - **ii.** Individual meets ONE of the following (a, b, or c):

a) Individual is treatment-naïve AND meets at least ONE of the following (1, 2, or 3):
  (1) Individual has compensated cirrhosis (Child-Pugh A) [includes individuals awaiting liver transplant]; OR
  (2) Individual does not have cirrhosis and baseline HCV RNA ≥ 6 million IU/mL (includes individuals awaiting liver transplant); OR
  (3) Individual has human immunodeficiency virus. OR
b) Individual has previously been treated for HCV and does not have cirrhosis; OR
c) Individual is treatment-naïve OR has previously been treated for HCV AND meets both of the following criteria (1 and 2):
  (1) Individual has decompensated cirrhosis (Child-Pugh B or C); AND
  (2) The medication will be prescribed in combination with ribavirin.

Note: This is a quantity sufficient to treat with one pellet packet per day for 12 weeks.

B) Approve 168 tablets per 365 days at retail or home delivery if the individual meets BOTH of the following criteria (i and ii):
i. Individual is < 12 years of age; AND
ii. Individual meets ONE of the following (a or b):
  a) Individual has previously been treated for HCV AND has compensated cirrhosis (Child-Pugh A); OR
  b) Individual is treatment-naïve OR has previously been treated for hepatitis C virus (HCV) AND meets both of the following criteria (1 and 2):
    (1) Individual has decompensated cirrhosis (Child-Pugh B or C);
    (2) Individual is ribavirin ineligible, according to the prescriber.

Note: This is a quantity sufficient to treat with one pellet packet per day for 24 weeks.

2. **Chronic Hepatitis C Virus Genotype 4, 5, or 6.** If the individual is < 12 years of age, approve 84 pellet packets per 365 days at retail or home delivery.
   Note: This is a quantity sufficient to teat with one pellet packet per day for 12 weeks.

3. **Recurrent Hepatitis C Virus Post-Liver Transplantation, Genotype 1 OR 4.** If the individual is < 12 years of age, approve 84 pellet packets per 365 days at retail or home delivery.
   Note: This is a quantity sufficient to treat with one pellet packet per day for 12 weeks.

4. For an indication or condition addressed as an approval in the above criteria section, approve the quantity requested, not to exceed 168 pellet packets per 365 days at retail or home delivery, to complete a course therapy.
   Note: For example, if the individual has received 4 weeks of therapy (28 pellet packets) and is eligible for 12 weeks of treatment, approve 56 tablets to complete 12 weeks of therapy. If an individual has received 4 weeks (28 pellet packets) of therapy and is eligible for 24 weeks of treatment, approve 140 tablets to complete 24 weeks of therapy.

Conditions Not Covered

Any other exception is considered not medically necessary.

Background

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.[1] It is indicated for the treatment of **chronic HCV** in patients ≥ 3 years of age in the following instances:

- 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 dosage of ledipasvir/sofosbuvir is one tablet (90 mg/400 mg) 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 (Table 1).[1] 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.

Table 1. Ledipasvir/sofosbuvir* Dosing in Pediatric Patients ≥ 3 Years of Age.[1]

Body Weight (kg)	Dose of Pellets or Tablets	Daily Dose of ledipasvir/sofosbuvir
< 17 kg	1 x 33.75 mg/150 mg packet of pellets QD	33.75 mg/150 mg
17 kg to < 35 kg	1 x 45 mg/200 mg packet of pellets QD; OR 1 x 45 mg/200 mg tablet QD	45 mg/200 mg
≥ 35 kg	2 x 45 mg/200 mg packets of pellets QD; OR 2 x 45 mg/200 mg tablets QD; OR 1 x 90 mg/400 mg tablet QD	90 mg/400 mg

* Only 90 mg/400 mg tablets are available as the authorized generic to Harvoni. All other dosage forms are available as Harvoni only (see Availability below); QD – Once daily

Availability

Harvoni is available as a tablet containing 90 mg of ledipasvir/400 mg sofosbuvir or 45 mg/ledipasvir/200 mg sofosbuvir.[1] It is also available as an oral pellet packet formulation containing 45 mg ledipasvir/200 mg sofosbuvir or 33.75 mg ledipasvir/150 mg sofosbuvir. The ledipasvir/sofosbuvir authorized generic is only available as the 90 mg/400 mg strength tablet. The table below provides the FDA recommended Harvoni treatment durations for treatment-naïve and treatment-experienced patients and those with and without cirrhosis.

Table 2. 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.

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 (January 2021).[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. For the most up-to-date information always refer to the guidelines.

Ledipasvir/sofosbuvir continues to be recommended in various situations as outlined below in Table 3.

Table 3. 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)	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)	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

Table 3 (continued). AASLD Recommendations for Harvoni.[2]

DAA	Duration	FDA Approved (Y/N)	AASLD Level of Evidence
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-Based Failure Only – 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 ≥ 12 years or ≥ 45 kg, ± Compensated Cirrhosis – Recommended			
ledipasvir/sofosbuvir	12 weeks	Y	Class I, Level B
Genotype 1, 4, 5, or 6 Treatment-Experienced Adolescents ≥ 12 years or ≥ 45 kg, ± Compensated Cirrhosis – Recommended			
ledipasvir/sofosbuvir	24 weeks (genotype 1 compensated cirrhosis)	Y	Class I, Level B
ledipasvir/sofosbuvir	12 weeks (GT 4, 5, or 6 ± compensated cirrhosis)	Y	Class I, Level B

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.

A quantity sufficient to allow for 8 weeks of therapy per 365 days will be covered without prior authorization. For coverage of additional quantities (for example, a 12 week or 24 week regimen), a coverage review is required.

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 October 5, 2021. Accessed on September 22, 2022.

Revision History

Type of Revision	Summary of Changes	Approval Date
Annual Revision	Policy was updated to include the existing quantity limits when the product is obtained via home delivery. **Ledipasvir/sofosbuvir 90 mg/400 mg tablets (Harvoni, generic).** For patients with genotype 1 chronic hepatitis C virus who are treatment-naïve or previously treated with decompensated cirrhosis, ribavirin ineligibility was modified to be according to the prescriber, previously stated as prescribing physician. For patients already started on therapy, criteria were clarified to approve a quantity not to exceed 168 tablets at retail or home delivery, previously no upper limit was specified. **Harvoni 45 mg/200 mg tablets and pellet packets.** Criteria for all override indications were modified to apply only to patients < 12 years of age, previously no age was specified. For patients with genotype 1 chronic hepatitis C virus who are treatment-naïve or previously treated with decompensated cirrhosis, ribavirin ineligibility was modified to be according to the prescriber, previously stated as prescribing physician. For recurrent hepatitis C virus post-liver transplantation, genotypes 5 and 6 were removed from the indication for approval, genotypes 1 and 4 remain approvable for overrides. Hepatitis C virus kidney transplant genotype 1 or 4 was removed as an indication approvable for overrides. For patients already started on therapy, criteria were clarified to approve a quantity not to exceed 336 tablets or pellet packets at retail or home delivery, previously no upper limit was specified. **Harvoni 33.75 mg/150 mg pellet packets.** Criteria for all override indications were modified to apply only to patients < 12 years of age, previously no age was specified. For patients with genotype 1 chronic hepatitis C virus who are treatment-naïve or previously treated with decompensated cirrhosis, ribavirin ineligibility was modified to be according to the prescriber, previously stated as prescribing physician. For recurrent hepatitis C virus post-liver transplantation, genotypes 5 and 6 were removed from the indication for approval, genotypes 1 and 4 remain approvable for overrides. Hepatitis C virus kidney transplant genotype 1 or 4 was removed as an indication approvable for overrides. For patients already started on therapy, criteria were clarified to approve a quantity not to exceed 168 pellet packets at retail or home delivery, previously no upper limit was specified.	09/28/2022