Harvoni (sofosbuvir/ledipasvir)

Override(s)	Approval Duration
Prior Authorization Quantity Limit	Based on genotype, treatment status, baseline HCV RNA status, cirrhosis status, transplant status, or ribavirin eligibility

Quantity Limit
1 tablet per day

APPROVAL DURATION

Based on Genotype, Treatment status, Baseline HCV RNA status, Cirrhosis Status, Transplant status, or Ribavirin eligibility

Genotype and Status (HCV mono-infected or HCV/HIV-1 co-infected[a])	Associated Treatment Regimens	Total Approval Duration of Harvoni
Genotype 1 (dual** or triple^ treatment-experienced, with prior sofosbuvir regimen, without compensated cirrhosis)	Harvoni + RBV	12 weeks
Genotype 1 (dual** or triple** treatment-experienced with prior sofosbuvir regimen, with compensated cirrhosis)	Harvoni + RBV	24 weeks
Genotype 4 (treatment-naïve, dual* treatment-experienced, or triple^ treatment-experienced, with or without compensated cirrhosis)	Harvoni	12 weeks
Genotype 1 (dual* or triple^ treatment-experienced, eligible for ribavirin, with compensated cirrhosis)	Harvoni + RBV	12 weeks
Genotype 1 or 4 (treatment-naïve or -experienced†, post-liver allograft transplant, with or without compensated cirrhosis)	Harvoni + RBV	12 weeks
Genotype 1 or 4 (treatment-naïve, post-liver allograft transplant, intolerant/ineligible for RBV, with or without compensated cirrhosis)	Harvoni	24 weeks
Genotype 1 or 4 (treatment-naïve or -experienced†, post-liver allograft transplant with decompensated cirrhosis)	Harvoni + RBV	12 weeks
Genotype 5 or 6 (treatment-naïve, dual treatment–experienced, or triple ^ treatment-experienced, with or without compensated cirrhosis)	Harvoni	12 weeks
Genotype 1 (treatment-naïve, baseline HCV RNA level of less than 6 million IU/mL, without compensated cirrhosis)	Harvoni	8 weeks
Genotype 1 (treatment-naïve, baseline HCV RNA level of greater than or equal to 6 million IU/mL, without compensated cirrhosis)	Harvoni	12 weeks
Genotype 1 (treatment-naïve, with compensated cirrhosis)	Harvoni	12 weeks
Genotype 1 (dual* or triple^ treatment-experienced, without compensated cirrhosis	Harvoni	12 weeks
Genotype 1 (dual* or triple^ treatment-experienced, with compensated cirrhosis)	Harvoni	24 weeks

**According to the June 2015 AASLD/IDSA updated treatment guidance, sofosbuvir and ribavirin or sofosbuvir and simeprevir define dual sofosbuvir treatment-experienced and sofosbuvir, ribavirin, and interferon define triple sofosbuvir treatment-experienced.
*Dual treatment-experienced refers to individuals who have had a partial response, no response, or prior relapse with a previous dual therapy regimen of interferon and ribavirin.
^Triple treatment-experienced refers to individuals who have had a partial response, no response, or prior relapse with a previous triple therapy regimen of Incivek or Victrelis, interferon, and ribavirin.
†AASLD/IDSA treatment guidance references the SOLAR-1 trial to support off-label recommendation in the post-liver transplant population. In the clinical trial, treatment-experienced was defined as a prior trial of interferon and ribavirin or a HCV protease inhibitor (Incivek, Victrelis, or Olysio), interferon, and ribavirin.

APPROVAL CRITERIA

Requests for Harvoni (sofosbuvir/ledipasvir) may be approved if the following criteria are met:

I. Individual is 18 years of age or older; **AND**
II. A copy of the baseline quantitative hepatitis C virus (HCV) RNA test result is provided to document baseline level of viremia; **AND**
III. Documentation is provided for a diagnosis of chronic hepatitis C (CHC) infection, which includes genotype[a] and a persistent positive HCV RNA test result for at least 6 months following positive baseline result (AASLD/IDSA 2015); **AND**
IV. Individual does not have a short life expectancy (less than 12 months owing to non-liver related comorbid conditions) that cannot be remediated by treating HCV, by transplantation or other directed therapy (AASLD/IDSA 2015); **AND**
V. Individual has one of the following (Label, AASLD/IDSA 2015):
   a. Genotypes 1, 4, 5, or 6 and compensated liver disease[1] (with or without cirrhosis); **OR**
   b. Genotypes 1 or 4 and decompensated liver disease[1] with cirrhosis following allograft liver transplantations

AND

VII. Individual meets **one** of the following:
   a. Individual is not actively abusing illicit drugs and/or alcohol; **OR**
   b. Individual is receiving concurrent treatment to facilitate cessation of drug and/or alcohol abuse (AASLD/IDSA 2015);

AND

VIII. Individual is using for **one** of the following antiviral treatment regimens:
   a. As monotherapy for **one** of the following:
      1. Individual is treatment-naïve, dual (interferon and ribavirin) treatment-experienced, or triple [interferon, ribavirin, and NS3 HCV protease inhibitor (Olysio, Incivek, or Victrelis)] treatment-experienced with or without compensated[1] cirrhosis and Genotype 1; **OR**
      2. Individual is treatment-naïve, dual (interferon and ribavirin) treatment-experienced, or triple [interferon, ribavirin, and NS3 HCV protease inhibitor (Olysio, Incivek, or Victrelis)] treatment-experienced with or without compensated[1] cirrhosis and Genotype 4; **OR**
      3. Individual is treatment-naïve, ribavirin intolerant/ineligible (such as but not limited to, pregnant women, hemoglobinopathies), with or without compensated[1] cirrhosis, and a post-liver allograft transplant recipient with HCV Genotypes 1 or 4 (AASLD/IDSA 2015); **OR**
      4. Individual is treatment-naïve, dual (interferon and ribavirin) treatment-experienced, or triple [interferon, ribavirin, and NS3 HCV protease inhibitor (Olysio, Incivek, or Victrelis)] treatment-experienced with or without compensated[1] cirrhosis and Genotypes 5 or 6;

   OR

   b. In combination with ribavirin for **one** of the following:
      1. Individual is dual (interferon and ribavirin) or triple [interferon, ribavirin, and NS3 HCV protease inhibitor (Olysio, Incivek, or Victrelis)] treatment-experienced with compensated[1] cirrhosis, eligible for ribavirin, and Genotype 1; **OR**

2. Individual is dual (sofosbuvir and ribavirin or sofosbuvir and simeprevir) or triple (interferon, ribavirin, and sofosbuvir) treatment-experienced with or without compensated[1] cirrhosis and Genotype 1 (AASLD/IDSA 2015); **OR**
3. Individual is treatment-naïve or treatment-experienced (interferon and ribavirin or interferon, ribavirin, and a NS3 HCV protease inhibitor), post-liver allograft transplant recipient with Genotypes 1 or 4 and compensated[1] liver disease with or without cirrhosis or decompensated[1] cirrhosis (AASLD/IDSA 2015).

Harvoni (sofosbuvir/ledipasvir) may not be approved for the following:

I. Individual has severe renal impairment (CrCl less than 30 mL/min), end stage renal disease, or requires dialysis; **OR**
II. Individual is requesting in concurrent therapy with contraindicated or not recommended agents, such as but not limited to the following: amiodarone, carbamazepine, phenytoin, phenobarbital, oxcarbazepine, rifabutin, rifampin, rifapentine, elvitegravir/cobicistat/emtricitabine/tenofovir DF, tipranavir/ritonavir, St John's Wort, or rosuvastatin; **OR**
III. Individual is using in combination with a non-nucleoside NS5B inhibitor (such as but not limited to dasabuvir) or another nucleotide NS5B polymerase inhibitor [such as Sovaldi (sofosbuvir)]; **OR**
IV. Individual is using in combination with another NS5A inhibitor [such as but not limited to, Daklinza (daclatasvir) or ombitasvir]; **OR**
V. Individual is using in combination with a NS3/4A protease inhibitor [such as but not limited to, Olysio (simeprevir), Incivek (telaprevir), Victrelis (boceprevir), or paritaprevir]; **OR**
VI. Individual is requesting the regimen for re-treatment and either failed to achieve a SVR (defined as a lower limit HCV RNA of 25 IU/mL) or relapsed after achieving a SVR during a prior successfully completed treatment regimen consisting of ledipasvir.

Notes:
[a] Per November 2015 FDA-approval and label update, Harvoni (ledipasvir/sofosbuvir) may be used in individuals who are co-infected with HIV-1. Concurrent use with all antiretroviral therapy is allowable with the exception of Aptivus (tipranavir)/ritonavir and Stribild (elvitegravir/cobicistat/emtricitabine/tenofovir DF).

1. **<u>Compensated Liver Disease</u>**:
   According to the American Association for the Study of Liver Diseases (AASLD, 2009, 2015), the specific criteria for compensated liver disease include all of the following: a total bilirubin; serum albumin; prothrombin time/INR; presence of ascites; and presence of hepatic encephalopathy. However, these criteria do not establish a comprehensive definition of compensated liver disease. The AASLD guidance refers to compensated liver disease as Class A based on the Child Pugh-Turcotte (CPT) classification scoring system.

Child Pugh Classification (AASLD/IDSA 2015)

Parameters			
Points Assigned	1 point	2 points	3 points
Total Bilirubin (µmol/L)	<34	34-50	>50
Serum Albumin (g/L)	>35	28-35	<28

Prothrombin time/INR	INR <1.7	1.71-2.30	>2.30
Ascites	None	Mild	Moderate to Severe
Hepatic Encephalopathy	None	Grade I-II (or suppressed with medication	Grade III-IV (or refractory)

Child Pugh Score Interpretation (AASLD/IDSA 2009, 2015)

Class A	5-6 points	Well compensated liver disease
Class B	7-9 points	Significant functional compromise (moderate hepatic impairment)
Class C	10-15 points	Uncompensated liver disease (severe hepatic impairment)

2. Scoring Systems for Fibrosis Staging (AASLD 2009):

Stage (F)	**IASL***	**Batts-Ludwig**	**Metavir**
0	No fibrosis	No fibrosis	No fibrosis
1	Mild fibrosis	Fibrosis portal expansion	Periportal fibrotic expansion
2	Moderate fibrosis	Rare bridges or septae	Periportal septae 1 (septum)
3	Severe fibrosis	Numerous bridges or septae	Porto-central septae
4	Cirrhosis	Cirrhosis	Cirrhosis

*IASL = The International Association for the Study of Liver

Stage (F)	**Ishak**
0	No fibrosis
1	Fibrosis expansion of some portal areas with or without short fibrous septa
2	Fibrous expansion of most portal areas with or without short fibrous septa
3	Fibrous expansion of most portal areas with occasional portal to portal bridging
4	Fibrous expansion of most portal areas with marked bridging (portal to portal and portal to central)
5	Marked bridging (portal to portal and portal to central) with occasional nodules (incomplete cirrhosis)
6	Cirrhosis

State Specific Mandates		
N/A	N/A	N/A

Key References:

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