Sovaldi (sofosbuvir)

Override(s)	Approval Duration
Prior Authorization	Based on Genotype, treatment status, cirrhosis status, hepatocellular carcinoma status, interferon/ribavirin eligibility status, or transplant status **OR** Genotype, treatment status, cirrhosis status, ribavirin eligibility status, or transplant status

Medication	Quantity Limit
Sovaldi (sofosbuvir)	1 tablet per day

APPROVAL DURATION

Based on Genotype, treatment status, cirrhosis status, hepatocellular carcinoma status, interferon/ribavirin eligibility status, or transplant status:

Genotype and Status type (HCV Mono-infected or HCV/HIV-1 Co-infected)	Associated Treatment Regimens	Total Approval Duration for Sovaldi
Genotype 1 (treatment-naïve or -experienced[#], post-liver allograft transplant, with or without compensated cirrhosis)	Sovaldi + Olysio ± RBV	12 weeks
Genotype 3 (treatment-naïve or -experienced*, post-liver allograft transplant, with or without compensated cirrhosis)	Sovaldi + RBV	24 weeks
Genotype 3 (post-liver allograft transplant, with decompensated cirrhosis)	Sovaldi + RBV	24 weeks
Genotype 1 (with or without compensated cirrhosis)	Sovaldi + IFN + RBV	12 weeks
Genotype 1 (treatment-naïve or dual treatment-experienced[+], without compensated cirrhosis)	Sovaldi +Olysio	12 weeks
Genotype 1a (treatment-naïve or dual treatment-experienced[+], with compensated cirrhosis, without Q80K polymorphism)	Sovaldi + Olysio ± RBV	24 weeks
Genotype 1b (treatment-naïve, or dual treatment-experienced[+] with compensated cirrhosis)	Sovaldi + Olysio ± RBV	24 weeks
Genotype 1 (treatment-naïve, with or without compensated cirrhosis, interferon ineligible)	Sovaldi + RBV	24 weeks
Genotype 2 (dual treatment-experienced[†*], with or without compensated cirrhosis, interferon eligible)	Sovaldi + IFN + RBV	12 weeks
Genotype 2 (treatment-naïve, with or without compensated cirrhosis)	Sovaldi +RBV	12 weeks^

Genotype 2 (dual treatment-experienced[†*], with or without compensated cirrhosis)	Sovaldi + RBV	16 weeks^
Genotype 3 (treatment-naïve or dual treatment-experienced[†+], with or without compensated cirrhosis)	Sovaldi + RBV	24 weeks
Genotype 3 (treatment naïve or dual treatment-experienced[*] with or without compensated cirrhosis, interferon eligible	Sovaldi + IFN + RBV	12 weeks
Genotype 4 (treatment-naïve or dual treatment-experienced[†]*, with or without compensated cirrhosis, interferon eligible)	Sovaldi + IFN + RBV	12 weeks
Genotype 4 (treatment-naïve or dual treatment-experienced[†*], with or without compensated cirrhosis)	Sovaldi + RBV	24 weeks
Genotype 5 or 6 (treatment-naïve, with or without compensated cirrhosis)	Sovaldi + IFN + RBV	12 weeks
Hepatocellular Carcinoma awaiting liver transplant	Sovaldi + RBV	Up to 48 weeks**

[#]Per the AASLD/IDSA 2015, support for Sovaldi and Olysio combination use in the liver post-transplant population is based on ongoing prospective studies in treatment-naïve and -experienced patients. Studies conducted in the treatment-experienced population mostly comprise prior regimens of interferon and ribavirin or interferon, ribavirin, and Incivek or Victrelis.
*A clinical trial completed with sofosbuvir and ribavirin following liver transplant recipients defines treatment-experienced in these specific populations as a prior failed trial of interferon and ribavirin; sofosbuvir and ribavirin; or interferon, ribavirin, and a HCV protease inhibitor (Incivek, Victrelis, or Olysio).
[+]Per Olysio label, treatment-experienced includes prior dual therapy (interferon and ribavirin) relapsers (HCV RNA not detected at the end of prior IFN-based therapy and detected during follow-up), prior partial responders (prior on-treatment ≥ 2 $\log_{10}$ IU/mL reduction in HCV RNA from baseline at Week 12 and HCV RNA detected at end of prior dual therapy) or prior null responders (prior on-treatment < 2 $\log_{10}$ reduction in HCV RNA from baseline at Week 12 during prior dual therapy).
[†*]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.
^ Therapy duration may be extended up to 8 additional weeks for a total of 24 weeks (AASLD/IDSA 2014).
** Therapy duration is recommended for up to 48 weeks or until the time of liver transplantation, whichever occurs first.

Based on Genotype, treatment status, cirrhosis status, ribavirin eligibility status, or transplant status

Genotype and Status (HCV mono-infected or HCV/HIV-1 co-infected[a])	**Associated Treatment Regimens**	**Total Approval Duration for Sovaldi**
Genotype 1 (treatment-naïve or -experienced[^], without compensated cirrhosis)	Sovaldi + Daklinza	12 weeks
Genotype 1 (treatment-naïve or -experienced[^], with compensated cirrhosis)	Sovaldi + Daklinza ± RBV	24 weeks
Genotype 2 (treatment-naïve, without compensated cirrhosis, ribavirin ineligible/intolerant)	Sovaldi + Daklinza	12 weeks
Genotype 2 (treatment-naïve, with compensated cirrhosis, ribavirin ineligible/intolerant)	Sovaldi + Daklinza	24 weeks
Genotypes 1, 2, 3, or 4 (treatment-naïve or -experienced[#], post-liver allograft transplant, with or without compensated cirrhosis)	Sovaldi + Daklinza + RBV	12 weeks
Genotypes 1, 2, 3, or 4 (treatment-naïve or -experienced[#] with decompensated cirrhosis)	Sovaldi + Daklinza + RBV	12 weeks
Genotype 3 (treatment-naïve or dual treatment-experienced*, with compensated cirrhosis)	Sovaldi + Daklinza + RBV	24 weeks
Genotype 3 (treatment-naive or dual treatment-experienced*, without compensated cirrhosis)	Sovaldi + Daklinza	12 weeks

^The August 2015 AASLD/IDSA treatment guidance update references clinical trials that define treatment-experienced in these specific populations as a prior failed trial of interferon and ribavirin or a HCV protease inhibitor (Incivek, Victrelis, or Olysio), interferon, and ribavirin.
#The August 2015 AASLD/IDSA treatment guidance update references clinical trials that define treatment-experienced in these specific populations as a prior failed trial of interferon and ribavirin; sofosbuvir and ribavirin; or interferon, ribavirin, and a HCV protease inhibitor (Incivek, Victrelis, or Olysio).
*Daklinza clinical trials conducted in these specific populations defined dual treatment-experienced as a prior trial with interferon ± ribavirin or sofosbuvir and ribavirin.

APPROVAL CRITERIA

Requests for Sovaldi (sofosbuvir) 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:
    a. Genotypes 1, 2, 3,4, 5, or 6 and compensated liver disease[1] (with or without cirrhosis; Label, AASLD/IDSA 2015); **OR**
    b. Genotypes 1,2,3, or 4 and decompensated[1] liver disease (with cirrhosis, AASLD/IDSA 2015);

AND
VI. 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
VII. Individual is using with **one** of the following antiviral treatment regimens:
    a. In combination with peg interferon and ribavirin for **one** of the following:
        1. Individuals with or without compensated[1] cirrhosis, Genotype 1, and has had a trial of Harvoni; **OR**
        2. Individual is dual (interferon and ribavirin) treatment-experienced with or without compensated[1] cirrhosis, eligible for interferon, and Genotype 2 (AASLD/IDSA 2015); **OR**
        3. Individual is treatment naïve or dual (interferon and ribavirin) treatment-experienced with or without compensated[1] cirrhosis, eligible for interferon, and Genotype 3 (AASLD/IDSA 2015); **OR**
        4. Individual is treatment-naïve or dual (interferon and ribavirin) treatment-experienced (AASLD/IDSA 2015) with or without compensated[1] cirrhosis, eligible for interferon, Genotype 4, and has had a trial of Harvoni; **OR**
        5. Individual is treatment-naïve with or without compensated[1] cirrhosis and Genotypes 5 or 6 (AASLD/IDSA 2015);

OR

b. In combination with ribavirin alone for **one** of the following:
    1. Individual is treatment-naïve with or without compensated cirrhosis, Genotype 1, a trial of Harvoni is clinically inappropriate (for example but not limited to, hypersensitivity), and is ineligible for an interferon-based regimen, as defined by the presence of **one** of the following:
        i. Intolerance to interferon (AASLD/IDSA 2015); **OR**
        ii. Autoimmune disorders (AASLD/IDSA 2015), including autoimmune hepatitis; **OR**
        iii. Child-Pugh score greater than 6 (Class B or C)[1] before or during interferon treatment; **OR**
        iv. Known hypersensitivity to interferon products; **OR**
        v. History of uncontrolled major depression, clinical features consistent with depression, or suicidal ideation (AASLD 2009, AASLD/IDSA 2015); **OR**
        vi. Uncontrolled epilepsy (EASL 2015); **OR**
        vii. Retinal disease (EASL 2015); **OR**
        viii. Baseline neutrophil count below 1500/µL, baseline platelet count below 90,000/µL or baseline hemoglobin below 10 g/dL (AASLD/IDSA 2015); **OR**
        ix. History of preexisting cardiac disease (AASLD/IDSA 2015);

    OR
    2. Individual is treatment-naïve or dual (interferon and ribavirin) treatment-experienced with or without compensated[1] cirrhosis and Genotype 2; **OR**
    3. Individual is treatment-naïve or dual (interferon and ribavirin) treatment-experienced with or without compensated[1] cirrhosis and Genotype 3; **OR**
    4. Individual is treatment-naïve or -experienced (interferon and ribavirin or interferon, ribavirin and a HCV protease inhibitor), post-liver allograft transplant, with or without compensated[1] cirrhosis and Genotype 3 (AASLD/IDSA 2015, Charlton et al. 2015); **OR**
    5. Individual is post-liver allograft transplant with decompensated[1] cirrhosis and Genotype 3 (AASLD/IDSA 2015); **OR**
    6. Individual is treatment naïve or dual (interferon and ribavirin) treatment-experienced with or without compensated[1] cirrhosis, Genotype 4 (AASLD/IDSA 2015), and has had a trial of Harvoni; **OR**
    7. Individuals with CHC and concurrent hepatocellular carcinoma meeting Milan criteria[b] (awaiting liver transplantation);

OR

c. In combination with Olysio (simeprevir) in individuals without compensated[1] cirrhosis and Genotype 1 who meet the following:
    1. Individual has had a trial of Harvoni: **AND**
    2. Individual is treatment-naïve or dual (interferon and ribavirin) treatment-experienced.

OR

d. In combination with Olysio (simeprevir) with or without ribavirin for the following:
    1. Individual has had a trial of Harvoni; **AND**
    2. Individual meets the following:

i. Individuals with Genotype 1a or 1b with compensated[1] cirrhosis; **AND**
ii. Individual is treatment-naïve or dual (interferon and ribavirin) treatment-experienced; **AND**
iii. Individual has been screened and is negative for the NS3Q80K polymorphism associated with HCV Genotype 1a subtype (AASLD/IDSA 2015);

OR

iv. Individual is treatment-naïve or -experienced (interferon and ribavirin or interferon, ribavirin, and Incivek or Victrelis), post-liver allograft transplant recipient with or without compensated1 cirrhosis, and Genotype 1 (AASLD/IDSA 2015);

OR

e. In combination with Daklinza (daclatasvir) for one of the following :
    1. Individual is treatment-naïve or -experienced (interferon and ribavirin or interferon, ribavirin and a HCV protease inhibitor) without compensated[1] cirrhosis, Genotype 1 (AASLD/IDSA 2015) and has had a trial of Harvoni; **OR**
    2. Individual is treatment-naïve with or without compensated[1] cirrhosis, ribavirin ineligible/intolerant (such as but not limited to, pregnant women, hemoglobinopathies), and Genotype 2 (AASLD/IDSA 2015); **OR**
    3. Individual is treatment-naïve or dual (interferon ± ribavirin or sofosbuvir + ribavirin) treatment-experienced without compensated[1] cirrhosis and Genotype 3 (Daklinza label);

OR

f. In combination with Daklinza (daclatasvir) with or without ribavirin (AASLD/IDSA 2015); **AND**
g. Individual is treatment-naïve or treatment-experienced (interferon and ribavirin or interferon, ribavirin, and a HCV protease inhibitor) with compensated[1] cirrhosis, Genotype 1, and has had a trial of Harvoni;

OR

h. In combination with Daklinza (daclatasvir) and ribavirin for one of the following (AASLD/IDSA 2015):
    1. Individual is treatment-naïve or -experienced (interferon and ribavirin; or interferon, ribavirin, and a HCV protease inhibitor), post-liver allograft transplant with or without compensated[1] cirrhosis, Genotypes 1 or 4, and has had a trial of Harvoni; **OR**
    2. Individual is treatment-naïve or -experienced (sofosbuvir and ribavirin), post-liver allograft transplant with or without compensated[1] cirrhosis and Genotypes 1 or 4; **OR**
    3. Individual is treatment-naïve or -experienced (interferon and ribavirin; sofosbuvir and ribavirin; or interferon, ribavirin, and a HCV protease inhibitor), post-liver allograft transplant with or without compensated[1] cirrhosis and Genotypes 2 or 3; **OR**

4. Individual is treatment-naïve or -experienced (interferon and ribavirin; sofosbuvir and ribavirin; or interferon, ribavirin, and a HCV protease inhibitor) with decompensated[1] cirrhosis, Genotypes 1 or 4; **OR**
5. Individual is treatment-naïve or -experienced (interferon and ribavirin; sofosbuvir and ribavirin; or interferon, ribavirin, and a HCV protease inhibitor) with decompensated[1] cirrhosis and Genotypes 2 or 3; **OR**
6. Individual is treatment-naïve or dual (interferon ± ribavirin or sofosbuvir + ribavirin) treatment-experienced with compensated[1] cirrhosis and Genotype 3.

Sovaldi (sofosbuvir) 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, St John's Wort, or tipranavir/ritonavir; **OR**
III. Individual is using in combination with a non-nucleoside NS5B polymerase inhibitor (such as but not limited to dasabuvir) or another nucleotide NS5B polymerase inhibitor (such as Harvoni [sofosbuvir/ledipasvir]); **OR**
IV. Individual is using in combination with a NS3/4A protease inhibitor other than Olysio (simeprevir) [such as but not limited to Incivek (telaprevir), Victrelis (boceprevir), or paritaprevir]; **OR**
V. Individual is using in combination with a NS5A inhibitor other than ledipasvir or Daklinza (daclatasvir) (such as but not limited to, ombitasvir); **OR**
VI. Individual is requesting for re-treatment in combination with Olysio (simeprevir) 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 a serine NS3/4A protease inhibitor (simeprevir, paritaprevir, or asunaprevir); **OR**
VII. Individual is requesting for re-treatment in combination with Olysio (simeprevir) 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 telaprevir or boceprevir, unless requested following post-liver allograft transplant); **OR**
VIII. Individual is requesting re-treatment in combination with Olysio (simeprevir) and either failed to achieve an SVR (defined as a lower limit HCV RNA of 25 IU/mL) or relapsed after achieving an SVR during a prior successfully completed treatment regimen consisting of sofosbuvir (such as Harvoni); **OR**
IX. Individual is requesting for re-treatment in combination with Daklinza (daclatasvir) 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 a NS5A inhibitor [such as but not limited to, Daklinza (daclatasvir), ledipasvir, or ombitasvir] (AASLD/IDSA 2015); **OR**
X. Individual is requesting for re-treatment in combination with Daklinza (daclatasvir) 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 paritaprevir (AASLD/IDSA 2015); **OR**

XI. Individual is requesting the regimen for re-treatment in combination with Daklinza (daclatasvir) 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 sofosbuvir, ribavirin, and interferon; **OR**

XII. Individual is requesting in combination with ribavirin or interferon and ribavirin and has received previous treatment for hepatitis C virus (HCV) with one of the following:
   a. An interferon-based triple therapy regimen, which includes ribavirin and a serene NS3/4A inhibitor [Incivek (telaprevir), Victrelis (boceprevir), or Olysio (simeprevir)], unless sofosbuvir and ribavirin are being requested following post-liver allograft transplant; **OR**
   b. An interferon-based triple therapy regimen, which includes ribavirin and Sovaldi (sofosbuvir); **OR**
   c. A therapy regimen containing a NS5A inhibitor [such as but not limited to, Harvoni (ledipasvir/sofosbuvir), Daklinza (daclatasvir), or ombitasvir]; **OR**
   d. A therapy regimen containing a serine NS3/4A protease inhibitor [such as but not limited to, Incivek (telaprevir), Victrelis (boceprevir), Olysio (simeprevir), paritaprevir, or asunaprevir]; **OR**
   e. A therapy regimen containing a NS5B polymerase inhibitor [such as but not limited to, Sovaldi (sofosbuvir), Harvoni (ledipasvir/sofosbuvir), or dasabuvir].

***Notes:**

[a]Per label and AASLD/IDSA 2015 treatment guidance, Sovaldi (sofosbuvir) may be used in individuals co-infected with human immunodeficiency virus (HIV)-1 either in combination with interferon and ribavirin (label), ribavirin (label), Olysio (simeprevir) (AASLD/IDSA 2015), or Daklinza (daclatasvir) (AASLD/IDSA 2015). Concurrent use of Sovaldi with all antiretroviral therapy is allowable with the exception of tipranavir/ritonavir.

[b] Milan criteria: A solitary tumor less than or equal to 5 cm or up to three (3) nodules less than or equal to 3 cm each with no extrahepatic manifestations or evidence of vascular invasion of tumor.

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	<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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