Epclusa (sofosbuvir/velpatasvir)

Overrides	Approval Duration
Prior Authorization Quantity Limit	Based on Age, Genotype, Treatment status, Cirrhosis status, Transplant status, Polymorphism status, or Ribavirin Eligibility status

Medication	Quantity Limit
Epclusa (sofosbuvir/velpatasvir) 200 mg/50 mg tablets	2 tablets per day
Epclusa (sofosbuvir/velpatasvir) 400 mg/100 mg tablets	1 tablet per day
Epclusa (sofosbuvir/velpatasvir) 200 mg/50 mg pellets	2 packets of pellets per day
Epclusa (sofosbuvir/velpatasvir) 150 mg/37.5 mg pellets	1 packet of pellets per day

APPROVAL DURATION

Genotype and Status (HCV mono-infected or HCV/HIV-1 co-infected[a])	Associated Treatment Regimens	Total Approval Duration of Epclusa
3 to 17 years of age, Genotypes 1, 2, 3, 4, 5, or 6 (treatment-naïve, dual P/R[2b] or triple[2d] treatment-experienced, with compensated cirrhosis or without cirrhosis)	Epclusa	12 weeks
3 to 17 years of age, Genotypes 1, 2, 3, 4, 5, or 6 (treatment-naïve, dual P/R[2b] or triple[2d] treatment-experienced, with decompensated cirrhosis)	Epclusa + RBV	12 weeks
Genotypes 1, 2, 4, 5, or 6 (treatment-naïve, dual P/R[2b] or triple[2d] treatment-experienced with compensated cirrhosis or without cirrhosis)	Epclusa	12 weeks
Genotypes 3 (dual P/R[2b] or triple[2d] treatment-experienced, with compensated cirrhosis or without cirrhosis)	Epclusa	12 weeks

Genotype 1, 2, 3, 4, 5, or 6, or Genotype unknown (acute HCV, treatment-naïve, without cirrhosis)	Epclusa	12 weeks
Genotype 3 (treatment-naïve, without cirrhosis)	Epclusa	12 weeks
Genotype 3 (treatment-naïve, with compensated cirrhosis, no Y93H polymorphism)	Epclusa	12 weeks
Genotype 3 (treatment-naïve, with compensated cirrhosis, with Y93H polymorphism)	Epclusa + RBV	12 weeks
Genotypes 1, 2, 3, 4, 5 or 6 (treatment-naïve or treatment-experienced without sofosbuvir or NS5A[2a], with decompensated cirrhosis)	Epclusa + RBV	12 weeks
Genotypes 1, 2, 3, 4, 5 or 6 (treatment-naïve or treatment-experienced without sofosbuvir or NS5A[2a], with decompensated cirrhosis, ineligible for ribavirin)	Epclusa	24 weeks
Genotypes 1, 2, 3, 4, 5 or 6 (treatment-experienced with sofosbuvir or NS5A[2a], with decompensated cirrhosis)	Epclusa + RBV	24 weeks
Genotypes 1, 2, 3, 4, 5, or 6 (post-liver allograft transplant recipient, treatment-naïve or treatment-experience, with compensated cirrhosis or without cirrhosis)	Epclusa	12 weeks
Genotypes 1, 2, 3, 4, 5, or 6 (post-liver allograft transplant recipient, treatment-naïve, with decompensated cirrhosis)	Epclusa + RBV	12 weeks
Genotypes 1, 2, 3, 4, 5, or 6 (post-liver allograft transplant recipient, treatment-experienced, with decompensated cirrhosis)	Epclusa + RBV	24 weeks
Hepatitis C-uninfected transplant recipient of a solid organ from a hepatitis C-positive donor (donor genotype 1, 2, 3, 4, 5, or 6, or genotype unknown)	Epclusa	12 weeks

APPROVAL CRITERIA

Requests for brand Epclusa (sofosbuvir/velpatasvir) are subject to **prior authorization** criteria only.

Requests for authorized generic Epclusa (sofosbuvir/velpatasvir) may be approved if the prior authorization criteria are met; **AND**

I. Documentation is provided that individual has had a prior trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response to brand Epclusa (sofosbuvir/velpatasvir); **AND**
   A. Documentation is provided describing the nature of the inadequate response or intolerance for each product;
      OR
   B. Documentation is provided that a completed FDA MedWatch Adverse Event Reporting Form has been submitted to the FDA for each product.

Prior Authorization Criteria:

I. Documentation is provided for a diagnosis of chronic hepatitis C (CHC) infection[a] which includes genotype and a positive HCV RNA result (AASLD/IDSA 2017, CDC 2013); **AND**
II. Individual has received baseline evaluation for liver fibrosis to guide appropriate therapy; **AND**
III. 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 2017); **AND**
IV. Individual has compensated[1] liver disease (with or without cirrhosis) or decompensated[1] liver disease;
AND
V. Individual is using in **one** of the following antiviral treatment regimens (Label/AASLD/IDSA 2021):
   A. Individual is 18 years of age or older, and using as monotherapy for **one** of the following:
      1. Individual is treatment-naïve or dual P/R[2b] or triple[2d] treatment-experienced with compensated[1] cirrhosis or without cirrhosis, and Genotypes 1, 2, 4, 5, or 6; **OR**
      2. Individual is dual P/R[2b] or triple[2d] treatment-experienced with compensated[1] cirrhosis or without cirrhosis and Genotype 3; **OR**
      3. Individual is treatment-naïve without cirrhosis, and Genotype 3; **OR**
      4. Individual is treatment-naïve with compensated[1] cirrhosis, and no polymorphism present at Y93H amino acid position, and Genotype 3; **OR**
      5. Individual is treatment-naïve or treatment-experienced without a sofosbuvir or NS5A[2a] containing regimen, ribavirin ineligible, with decompensated[1] cirrhosis, and Genotypes 1, 2, 3, 4, 5 or 6; **OR**
      6. Individual is post-liver allograft transplant recipient, treatment-naïve or treatment-experienced, with compensated[1] cirrhosis or without cirrhosis, and Genotype 1, 2, 3, 4, 5, or 6;

   OR

   B. Individual is 18 years of age or older, and using in combination with ribavirin for **one**

of the following:

1. Individual is treatment-naïve with compensated[1] cirrhosis, with polymorphism present at Y93H amino acid position, and Genotype 3; **OR**
2. Individual is treatment-naïve or treatment-experienced, with decompensated[1] cirrhosis, and Genotypes 1, 2, 3, 4, 5 or 6; **OR**
3. Individual is a post-liver allograft transplant recipient, treatment-naïve or treatment-experienced, with decompensated[1] cirrhosis, and Genotypes 1, 2, 3, 4, 5, or 6;

OR

C. Individual is 3 to 17 years of age and is using for one of the following:
   1. As monotherapy for treatment-naïve, dual P/R[2b] or triple[2d] treatment-experienced, with compensated[1] cirrhosis or without cirrhosis, and Genotypes 1, 2, 3, 4, 5, or 6; **OR**
   2. In combination with ribavirin for treatment-naïve, dual P/R[2b] or triple[2d] treatment-experienced, with decompensated[1] cirrhosis, and Genotypes 1, 2, 3, 4, 5, or 6; **OR**
   3. Individual is a post-liver allograft transplant recipient, treatment-naïve or treatment-experienced, with compensated[1] cirrhosis or without cirrhosis, and Genotype 1, 2, 3, 4, 5, or 6;

OR

VI. Individual is 3 years of age or older, and meets all of the following (AASLD/IDSA 2019):
   A. Documentation is provided for a diagnosis of acute hepatitis C infection[a], which includes a positive HCV RNA result, and with or without genotype; **AND**
   B. Individual has received baseline evaluation for liver fibrosis to guide appropriate therapy; **AND**
   C. 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; **AND**
   D. Individual is treatment-naïve, without cirrhosis, and Genotype 1, 2, 3, 4, 5, or 6, or genotype is unknown;

OR

VII. Individual is 3 years of age or older, and meets all of the following (AASLD/IDSA 2020):
   A. Individual is hepatitis C-negative; **AND**
   B. Individual is a transplant recipient of a solid organ from a hepatitis C-positive donor; **AND**
   C. Donor genotype is 1, 2, 3, 4, 5, or 6, or genotype is unknown.

Epclusa (sofosbuvir/velpatasvir) may **not** be approved for the following:

I. Individual is requesting in concurrent therapy with contraindicated or not recommended agents, including but not limited to amiodarone, carbamazepine, phenytoin, phenobarbital, oxcarbazepine, rifabutin, rifampin, rifapentine, St John's Wort, tipranavir/ritonavir, topotecan, efavirenz, etravirine, nevirapine, or lumacaftor; **OR**

II. Individual is using in combination with a regimen containing a non-nucleoside NS5B polymerase inhibitor (such as dasabuvir) or another nucleotide NS5B polymerase inhibitor; **OR**

III. Individual is using in combination with another regimen containing a NS5A[2a] inhibitor; **OR**

IV. Individual is using in combination with a regimen containing a NS3/4A[2c] protease inhibitor; **OR**

V. 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 sofosbuvir/velpatasvir/voxilaprevir.

Notes:

[a]Per label and AASLD/IDSA treatment guidance, Epclusa (sofosbuvir/velpatasvir) may be used in individuals who are co-infected with HIV-1. The AASLD/IDSA treatment guidance recommends that concurrent use with tenofovir disoproxil fumarate (TDF) should be avoided with an eGFR below 60 mL/min.

1. **Compensated Liver Disease**:
   According to the American Association for the Study of Liver Diseases (AASLD/IDSA2017), 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.

   Moderate to Severe (Decompensated) Liver Disease:
   The AASLD guidance refers to decompensated (moderate to severe) liver disease as Class B or C based on the Child-Pugh Turcotte (CPT) classification scoring system.

Child Pugh Classification (AASLD/IDSA 2017)

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 2017)

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. Past Treatment Exposure Definitions (AASLD/IDSA 2017):
   a. NS5A Inhibitor: includes daclatasvir, ledipasvir, elbasvir, ombitasvir, pibrentasvir, or velpatasvir-containing regimens
   b. P/R: includes peginterferon (or non-pegylated interferon) ± ribavirin
   c. NS3/4A Protease Inhibitor: includes simeprevir, grazoprevir, paritaprevir, glecaprevir, and voxilaprevir-containing regimens
   d. Triple therapy: includes NS3 protease inhibitor (simeprevir, boceprevir or telaprevir) plus peginterferon and ribavirin
   e. Direct Acting Antiviral (DAA): includes NS5A inhibitors, NS3/4A protease inhibitors, and
      NS5B polymerase inhibitors (sofosbuvir, dasabuvir)
   f. P/R/S: includes peginterferon (or non-pegylated interferon) ± ribavirin ± sofosbuvir

3. Chronic Kidney Disease (CKD) Definitions (AASLD/IDSA 2017):
   Severe CKD (Stage 4): eGFR 15-29 mL/min
   End-Stage CKD (Stage 5): eGFR < 15 mL/min

4. **Metavir Scoring Systems for Fibrosis Staging (AASLD 2009):**

Stage (F)	
0	No fibrosis
1	Periportal fibrotic expansion
2	Periportal septae 1 (septum)
3	Porto-central septae
4	Cirrhosis

5. Hepatitis C virus (HCV) direct acting antiviral (DAA) agents have a black box warning for risk of hepatitis B virus (HBV) reactivation in individuals with HCV-HBV co-infection. Individuals should be tested for evidence of current or prior HBV infection prior to initiation of DAA therapy. HBV reactivation has been reported in HCV/HBV co-infected individuals currently taking or previously completed DAA therapy and not concomitantly receiving HBV antiviral therapy. Some cases of HBV reactivation have led to fulminant hepatitis, hepatic failure, and death. Individuals should be monitored for hepatitis flare or HBV reactivation during and following HCV DAA therapy. Individuals should be appropriately managed for HBV infection as indicated.

Key References:

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3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.

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5. American Association for the Study of Liver Diseases and the Infectious Disease Society of America, in collaboration with the International Antiviral Society-USA. Recommendations for testing, managing and treating hepatitis C. Available at http://www.hcvguidelines.org/. Published on: January 29, 2014. Updated on: September 29, 2021. Accessed on: January 26, 2022.
6. Centers for Disease Control and Prevention. Testing for HCV Infection: An Update of Guidance for Clinicians and Laboratorians. *MMWR*. 2013; 62(18):362-365. Available from: https://www.cdc.gov/mmwr/pdf/wk/mm6218.pdf. Accessed on: January 26, 2022.
7. Kamal SM. Acute hepatitis C: a systematic review. Am J Gastroenterol. 2008;103(5):1283-1297.
8. U.S. Department of Health and Human Services AIDSinfo treatment guidelines. Considerations for Antiretroviral Use in Patients with Coinfections. Available at https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/26/hcv-hiv. Accessed on: January 13, 2021.
9. Wyles D, Weiland O, Yao B, et al. Retreatment of patients who failed glecaprevir/pibrentasvir treatment for hepatitis C virus infection. J Hepatol. 2019;70(5):1019-1023.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.