Epclusa (sofosbuvir/velpatasvir)

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

Medication	Quantity Limit
Epclusa (sofosbuvir/velpatasvir) 400 mg/100 mg	1 tablet 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
Genotypes 1, 2, 4, 5, or 6 (treatment- naïve, dual P/R[2b] treatment-experienced, or triple[2d] treatment-experienced with compensated cirrhosis or without cirrhosis)	Epclusa	12 weeks
Genotype 1b (previous sofosbuvir containing regimen without an NS5A[2a], with compensated cirrhosis or without cirrhosis)	Epclusa	12 weeks
Genotype 2 (sofosbuvir plus ribavirin treatment-experienced, with compensated cirrhosis or without cirrhosis)	Epclusa	12 weeks
Genotype 3 (treatment-naïve, with compensated cirrhosis or without cirrhosis, no Y93H polymorphism)	Epclusa	12 weeks
Genotype 3 (dual P/R[2b] treatment-experienced, without cirrhosis, no Y93H polymorphism)	Epclusa	12 weeks
Genotype 3 (dual P/R[2b] treatment-experienced, with compensated 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)	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 2 or 3 (post-liver allograft transplant recipient, with compensated or decompensated cirrhosis)	Epclusa + RBV	12 weeks

APPROVAL CRITERIA

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

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

I. Individual has had a prior trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response to authorized generic Epclusa (sofosbuvir/velpatasvir); **OR**
II. Individual is currently on and completing a course of therapy with the requested regimen.

Prior Authorization Criteria:

I. Individual is 18 years of age or older; **AND**
II. 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**
III. Individual has received baseline evaluation for liver fibrosis to guide appropriate therapy; **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 2017); **AND**

V. Individual is supervised by a gastroenterologist OR infectious disease specialist **OR** a physician specialized in hepatitis treatment and management **OR** a physician working in consultation with gastroenterologist or infectious disease specialist; **AND**
VI. Individual has liver fibrosis of Metavir score F2 or greater **AND**
VII. Individual has compensated[1] liver disease (with or without cirrhosis) or decompensated[1] liver disease;

AND
VIII. Individual is using in **one** of the following antiviral treatment regimens (AASLD/IDSA 2017) :
A. As monotherapy for **one** of the following:
1. Individual is treatment-naïve or dual P/R[2b] treatment- experienced, or triple[2d] treatment-experienced with compensated[1] cirrhosis or without cirrhosis, and Genotypes 1, 2, 4, 5, or 6; **OR**
2. Individual is treatment experienced with a sofosbuvir-containing regimen without an NS5A[2b] inhibitor with compensated[1] cirrhosis or without cirrhosis, and Genotype 1b; **OR**
3. Individual is sofosbuvir plus ribavirin treatment-experienced with compensated[1] cirrhosis or without cirrhosis, and Genotype 2; **OR**
4. Individual is treatment-naïve with compensated[1] cirrhosis or without cirrhosis or dual P/R[2b] treatment-experienced without cirrhosis, no Y93H polymorphism, 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
B. In combination with ribavirin for one of the following:
1. Individual is dual P/R[2b] treatment-experienced, with compensated[1] cirrhosis, 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, with compensated[1] or decompensated[1] cirrhosis, and Genotypes 2 or 3.

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

I. Individual has severe or end stage CKD[3] or requires dialysis; **OR**
II. Individual is requesting in concurrent therapy with contraindicated or not recommended agents, such as 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**
III. 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**

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

V. Individual is using in combination with a regimen containing a NS3/4A[2c] protease inhibitor; **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 sofosbuvir/velpatasvir/voxilaprevir.

Notes:

[a]Per labeland 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)

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.

State Specific Mandates		
State/Market	**Date**	**Description**
Georgia Medicaid	10/2016	Georgia has state mandated criteria; please see Georgia State Specific Criteria.
Louisiana Medicaid	2/1/2018	Louisiana has state criteria; please see Louisiana State Specific Criteria

Maryland Medicaid		Maryland has state mandated criteria; please see Maryland State Specific Criteria
Virginia Medicaid	7/1/2016	Virginia has state mandated criteria; please see Virginia State Specific Criteria.
Washington D.C.	2/1/2018	Washington D. C. has state criteria; please see Washington D. C. State Specific Criteria

Key References:

1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2019. URL: http://www.clinicalpharmacology.com. Updated periodically.
2. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: January 4, 2019.
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2019; Updated periodically.
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: May 24, 2018. Accessed on: December 28, 2018.
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 4, 2019.
7. European Association for the Study of the Liver. EASL Recommendations on Treatment of Hepatitis C 2018. *J Hepatol*. 2018; https://doi.org/10.1016/jhep.2018.03.026. Available from: http://www.easl.eu/research/our-contributions/clinical-practice-guidelines/detail/easl-recommendations-on-treatment-of-hepatitis-c-2018. Accessed on: January 4, 2019.
8. U.S. Department of Health and Human Services AIDSinfo treatment guidelines. Concomitant use of selected antiretroviral drugs and hepatitis C virus direct-acting antiviral drugs for treatment of HCV in adults with HIV. Available at https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/26/hcv-hiv. Accessed on: January 3, 2019.