# Epclusa (sofosbuvir/velpatasvir)

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

| 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 |



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| | | |
|---|---|---|
| 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 Epclusa (sofosbuvir/velpatasvir) may be approved if the following criteria are met:

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, a reactive HCV antibody, and a subsequent positive HCV RNA result to confirm diagnosis (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. Individuals who abuse alcohol or intravenous drugs must be enrolled in a substance abuse program; **AND**
VI. Individual has compensated[1] liver disease (with or without cirrhosis) or decompensated[1] liver disease;

**AND**

VII. 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; **AND**

       For Genotype 1, 2, 5, 6:
    2. Individual has had a prior trial (medication samples/coupons/discount cards are excluded


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from consideration as a trial) and inadequate response to Mavyret; **OR**

a. Individual is currently on and completing a course of therapy with the requested regimen; **OR**
b. Documented hypersensitivity, as manifested by a severe allergic reaction, to any ingredient in Mavyret which is not also in Epclusa; **OR**
c. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimens;

**OR**

3. 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**
4. Individual is sofosbuvir plus ribavirin treatment-experienced with compensated[1] cirrhosis or without cirrhosis, and Genotype 2
   **OR**
5. Individual is treatment-naïve with compensated[1] cirrhosis or without cirrhosis, no Y93H polymorphism, and Genotype 3; **AND**
6. Individual has had a prior trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response to Mavyret; **OR**
   a. Individual is currently on and completing a course of therapy with the requested regimen; **OR**
   b. Documented hypersensitivity, as manifested by a severe allergic reaction, to any ingredient in Mavyret which is not also in Epclusa; **OR**
   c. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimens;

**OR**

7. Individual is dual P/R[2b] treatment-experienced without cirrhosis, no polymorphism present at Y93H amino acid position, and Genotype 3;

**OR**

8. Individual is treatment-naïve, dual P/R[2b] treatment-experienced, or triple treatment-experienced with decompensated[1] cirrhosis, ribavirin ineligible, and Genotypes 1, 2, 3, 4, 5 or 6;

**OR**

B. In combination with ribavirin for one of the following:



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1. Individual is dual P/R[2b] treatment-experienced, with compensated[1] cirrhosis, and Genotype 3; **OR**
2. Individual is treatment-naïve, dual P/R[2b] treatment- experienced, or triple[2d] treatment-experienced with decompensated[1] cirrhosis, and Genotypes 1, 2, 3, 4, 5 or 6; **OR**
3. Individual is sofosbuvir or NS5A2a treatment-experienced with decompensated[1] cirrhosis, and Genotypes 1, 2, 3, 4, 5, or 6; **OR**
4. Individual is a post-liver allograft transplant recipient, with decompensated[1] cirrhosis, and Genotypes 2 or 3;

**OR**

5. Individual is a post-liver allograft transplant recipient, with compensated[1] cirrhosis, and Genotypes 2 or 3; **AND**
6. Individual has had a prior trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response to Mavyret; **OR**
    a. Individual is currently on and completing a course of therapy with the requested regimen; **OR**
    b. Documented hypersensitivity, as manifested by a severe allergic reaction, to any ingredient in Mavyret which is not also in Epclusa; **OR**
    c. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimens.

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.



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**Notes**:
[a]Per label, 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)


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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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