Mavyret
(glecaprevir/pibrentasvir)

Override(s)	Approval Duration
Prior Authorization Quantity Limit	Based on Genotype, Treatment status, Cirrhosis status, or Transplant status.

Medication	Quantity Limit
Mavyret (glecaprevir/pibrentasvir) 100 mg/40 mg tablets	3 tablets per day
Mavyret (glecaprevir/pibrentasvir) 50 mg/20 mg pellets*	5 packets of pellets per day*

*For Mavyret 50 mg/20 mg pellets: May approve 6 packets of pellets per day (max dose of 300 mg/120 mg per day) based on the following criteria:

I. Individual weighs 45 kg or greater; **AND**
II. Individual is unable to swallow tablets.

APPROVAL DURATION

Genotype and Status (HCV mono-infected or HCV/HIV-1 co-infected[a])	Associated Treatment Regimens	Total Approval Duration of Mavyret
Genotypes 1, 2, 3, 4, 5, or 6 (treatment-naïve, with compensated cirrhosis or without cirrhosis)	Mavyret	8 weeks
Genotypes 1, 2, 3, 4, 5, or 6, or Genotype unknown (acute HCV, treatment-naïve, without cirrhosis)	Mavyret	8 weeks
Genotype 1 (treatment-experienced with an NS5A[2a] inhibitor and without prior treatment with an NS3/4A[2c] protease inhibitor, with compensated cirrhosis or without cirrhosis)	Mavyret	16 weeks
Genotype 1 (treatment-experienced with an NS3/4A[2c] protease inhibitor or sofosbuvir and without prior treatment with an NS5A[2a] inhibitor, with compensated cirrhosis or without cirrhosis)	Mavyret	12 weeks
Genotype 3 (dual P/R[2b] treatment-experienced, or experienced with	Mavyret	16 weeks

sofosbuvir-containing regimen, without NS3/4A[2c] or NS5A[2a], with compensated cirrhosis or without cirrhosis)		
Genotypes 1, 2, 4, 5, or 6 (dual P/R[2b] treatment-experienced, or P/R/S[2f] experienced without cirrhosis)	Mavyret	8 weeks
Genotypes 1, 4, 5, and 6 (dual P/R[2b] treatment-experienced, or P/R/S[2f] experienced with compensated cirrhosis)	Mavyret	12 weeks
Genotype 1, 2, 4, 5, or 6 (treatment experienced with sofosbuvir containing regimen, without NS3/4A[2c], with compensated cirrhosis or without cirrhosis)	Mavyret	16 weeks
Genotypes 1, 2, 3, 4, 5, or 6 (treatment failure with Mavyret [glecaprevir/pibrentasvir] monotherapy, with compensated cirrhosis or without cirrhosis)	Mavyret + Sovaldi + RBV	16 weeks
Genotype 1, 2, 4, 5, or 6 (previous treatment failure with Vosevi [sofosbuvir/velpatasvir/voxilaprevir]) with compensated cirrhosis or without cirrhosis	Mavyret + Sovaldi + RBV	16 weeks
Genotype 3 (previous treatment failure with Vosevi [sofosbuvir/velpatasvir/voxilaprevir]) without cirrhosis	Mavyret + Sovaldi + RBV	16 weeks
Genotype 3 (previous treatment failure with Vosevi [sofosbuvir/velpatasvir/voxilaprevir]) with compensated cirrhosis	Mavyret + Sovaldi + RBV	24 weeks
Genotype 1, 2, 3, 4, 5, or 6 (previous treatment failure with Sovaldi plus Mavyret [sofosbuvir/glecaprevir/pibrentasvir]) with compensated cirrhosis or without cirrhosis	Mavyret + Sovaldi + RBV	24 weeks

Genotypes 1, 2, 3, 4, 5, or 6 (treatment-naïve or treatment-experienced, post-liver allograft transplant recipient, with compensated cirrhosis or without cirrhosis)	Mavyret	12 weeks
Genotype 1 (NS5A[2a] inhibitor-experienced without prior treatment with an NS3/4A[2c] protease inhibitor, post-liver or post-kidney transplant recipient, with compensated cirrhosis or without cirrhosis)	Mavyret	16 weeks
Genotype 3 (P/R/S[2f] treatment-experienced, post-liver or post kidney transplant recipient, with compensated cirrhosis or without cirrhosis)	Mavyret	16 weeks
Genotypes 1, 2, 3, 4, 5, or 6 (treatment-naïve or treatment-experienced, post-kidney transplant recipient, with compensated cirrhosis or without cirrhosis)	Mavyret	12 weeks
Hepatitis C-uninfected transplant recipient of a liver from a hepatitis C-positive donor (donor genotype 1, 2, 3, 4, 5, or 6, or genotype unknown)	Mavyret	12 weeks
Hepatitis C-uninfected transplant recipient of a non-liver solid organ from a hepatitis C-positive donor (donor genotype 1, 2, 3, 4, 5, or 6, or genotype unknown)	Mavyret	8 weeks

APPROVAL CRITERIA

Requests for Mavyret (glecaprevir/pibrentasvir) may be approved if the following criteria are met:

I. Individual is 3 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 has compensated[1] liver disease (with or without cirrhosis);

AND

VI. 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) unless one of the following conditions apply:

A. Individual is using in **one** of the following antiviral treatment regimens (Label/AASLD/IDSA 2021):
   1. As monotherapy for **one** of the following:
      a. Individual is treatment-naïve, with compensated[1] cirrhosis or without cirrhosis, and Genotypes 1, 2, 3, 4, 5, or 6; **AND**
      b. Individual meets one of the following criteria:
         i. Prior trial of brand Epclusa with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Mavyret; **OR**
         ii. Individual is currently on and completing a course of therapy with Mavyret; **OR**
         iii. 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 regimen or regimens; **OR**
         iv. Individual is treatment-naïve, with compensated[1] cirrhosis, with Y9H3 polymorphism, Genotype 3**;

OR

      c. Individual is treatment-experienced with a prior HCV NS5A[2a] inhibitor regimen without prior HCV treatment with an NS3/4A[2c] protease inhibitor with compensated[1] cirrhosis or without cirrhosis, and Genotype 1;

OR

      d. Individual is treatment-experienced with a prior HCV NS3/4A[2c] protease inhibitor regimen without prior HCV treatment with an NS5A[2a] inhibitor, with compensated[1] cirrhosis or without cirrhosis, and Genotype 1;

OR

      e. Individual is dual P/R[2b] treatment-experience with compensated[1] cirrhosis or without cirrhosis, and Genotypes 1, 2, 3, 4, 5, or 6; **AND**
      f. Individual meets one of the following criteria:
         i. Prior trial of brand Epclusa with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Mavyret; **OR**
         ii. Individual is currently on and completing a course of therapy with Mavyret; **OR**
         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 regimen or regimens;

OR

      g. Individual is P/R/S[2f] experienced with compensated[1] cirrhosis or without cirrhosis, and Genotypes 1, 2, 3, 4, 5, or 6;

OR

h. Individual is experienced with sofosbuvir-containing regimen, without NS3/4A2c or NS5A2a, with compensated[1] cirrhosis or without cirrhosis, and Genotypes 3;

OR

i. Individual is treatment experienced with sofosbuvir-containing regimen, without NS3/4A[2c], with compensated[1] cirrhosis or without cirrhosis, and Genotype 1, 2, 4, 5, or 6;

OR

j. Individual is a post-liver allograft transplant recipient with compensated[1] cirrhosis or without cirrhosis, and Genotypes 1, 2, 3, 4, 5, or 6; **AND**

k. Individual meets one of the following criteria:

i. Prior trial of brand Epclusa with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Mavyret; **OR**

ii. Individual is currently on and completing a course of therapy with Mavyret; **OR**

iii. 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 regimen or regimens;

OR

l. Individual is a post-kidney transplant recipient, with or without compensated[1] cirrhosis, and Genotypes 1, 2, 3, 4, 5, or 6;

OR

2. In combination with Sovaldi (sofosbuvir) and ribavirin for the following (AASLD/IDSA 2021):

a. Individual had prior treatment failure with Mavyret (glecaprevir/pibrentasvir) monotherapy, and Genotype 1, 2, 3, 4, 5, or 6, with compensated[1] cirrhosis or without cirrhosis; **OR**

b. Individual had treatment failure with Vosevi [sofosbuvir/velpatasvir/voxilaprevir], with compensated[1] cirrhosis or without cirrhosis, and Genotype 1, 2, 3, 4, 5, or 6; **OR**

c. Individual had treatment failure with Sovaldi plus Mavyret [sofosbuvir/glecaprevir/pibrentasvir]) with compensated[1] cirrhosis or without cirrhosis, and Genotype 1, 2, 3, 4, 5, or 6;

OR

VII. Individual is 3 years of age or older (AASLD/IDSA 2019); **AND**

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: **AND**

E. 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) unless one of the following conditions apply:
    1. Prior trial of brand Epclusa with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Mavyret; **OR**
    2. Individual is currently on and completing a course of therapy with Mavyret; **OR**
    3. 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 regimen or regimens**.**

OR

VIII. Individual is 3 years of age or older, and meets all of the following (AASLD/IDSA 2020):
A. Individual is hepatitis C-uninfected; **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; **AND**
D. Individual has had a prior trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response to brand Epclusa unless one of the following conditions apply:
    1. Prior trial of brand Epclusa with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Mavyret, and documentation is provided; **OR**
    2. Individual is currently on and completing a course of therapy with Mavyret; **OR**
    3. 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 regimen or regimens.

Mavyret (glecaprevir/pibrentasvir) may **not** be approved for the following:

I. Individual has decompensated[1] cirrhosis, or any history of prior hepatic decompensation; **OR**
II. Individual is requesting in concurrent therapy with contraindicated or not recommended agents, including but not limited to ritonavir-containing antiretroviral regimens, efavirenz, etravirine, nevirapine, darunavir/cobicistat, atazanavir, carbamazepine, St John's wort, ethinyl estradiol-containing medications, atorvastatin, lovastatin, simvastatin, and rifampin; **OR**
III. Individual is using in combination with a regimen containing a non-nucleoside NS5B polymerase inhibitor (such as dasabuvir); **OR**
IV. Individual is using in combination with a regimen containing another NS5A[2a] inhibitor; **OR**
V. Individual is using in combination with a regimen containing another 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 elbasvir/grazoprevir, ombitasvir/paritaprevir/ritonavir or dasabuvir/ombitasvir/paritaprevir/ritonavir.

Notes:

[a]Per label and AASLD/IDSA treatment guidance, Mavyret (glecaprevir/pibrentasvir) may be used in individuals who are co-infected with HIV-1.

**Individual has a unique disease characteristic to which the preferred regimen(s) is not recommended (examples include specific genotype subtype, resistance-associated substitution [RAS], or polymorphism).

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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