PRIOR AUTHORIZATION POLICY

POLICY: Hepatitis C – Mavyret Prior Authorization Policy
- Mavyret™ (glecaprevir/pibrentasvir tablets – AbbVie)

REVIEW DATE: 08/19/2020

OVERVIEW

Mavyret, a direct-acting antiviral, is indicated for the treatment of adult and pediatric patients ≥ 12 years of age or ≥ 45 kg with chronic hepatitis C virus (HCV) genotype 1, 2, 3, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis (Child-Pugh A).[1] Mavyret is also indicated for the treatment of adult and pediatric patients ≥ 12 years of age or ≥ 45 kg with HCV genotype 1 infection who previously have been treated with a regimen containing an HCV NS5A inhibitor or an NS3/4A protease inhibitor, but not both.[1] Mavyret contains glecaprevir, a new pangenotypic NS3/4A protease inhibitor and pibrentasvir, a new pangenotypic NS5A inhibitor.

Dosing

The recommended dose of Mavyret is three tablets (total daily dose: glecaprevir 300 mg and pibrentasvir 120 mg) taken once daily with food. No dosage adjustments are required for patients with human immunodeficiency virus (HIV) co-infection and/or chronic kidney disease, including dialysis. The duration of therapy is based on prior treatment experience, genotype, and the presence or absence of cirrhosis (see Table 1). Mavyret is recommended for 12 weeks in adults and pediatric patients ≥ 12 years of age or ≥ 45 kg liver or kidney transplant recipients. Similar to non-transplant recipients, a 16-week treatment duration is recommended in genotype 1-infected patients who are NS5A inhibitor-experienced without prior treatment with an NS3/4A protease inhibitor or in genotype 3-infected patients who are treatment experienced with regimens containing interferon, pegylated interferon, ribavirin, and/or Sovaldi® (sofosbuvir tablets).

Table 1. Recommended Duration for Treatment-Naïve Patients.[1]

HCV Genotype	Treatment Duration	
	No Cirrhosis	Compensated Cirrhosis (Child-Pugh A)
1, 2, 3, 4, 5, or 6	8 weeks	8 weeks

HCV – Hepatitis C virus.

Table 2. Recommended Duration for Treatment-Experienced Patients.[1]

HCV Genotype	Prior Treatment Experience	Duration	
		Without Cirrhosis	With Compensated Cirrhosis
1, 2, 4, 5, 6	PRS	8 weeks	12 weeks
3	PRS	16 weeks	16 weeks
1	NS3/4 PI[1] (NS5A-naïve)	12 weeks	12 weeks
	NS5A inhibitor[2] (NS3/4 PI-naïve)†	16 weeks	16 weeks

HCV – Hepatitis C virus; PRS – Prior treatment experience with regimens containing interferon, pegylated interferon, ribavirin, and/or Sovaldi® (sofosbuvir tablets), but no prior treatment experience with an HCV NS3/4A protease inhibitor (PI) or NS5A inhibitor; PI – Protease inhibitor; [1] Regimens containing Olysio® (simeprevir capsules) and Sovaldi, or Olysio, Victrelis® (boceprevir capsules), or Incivek® (telaprevir tablets) with interferon or pegylated interferon and ribavirin were studied; [2] Regimens containing Harvoni® (ledipasvir/sofosbuvir tablets) or Daklinza® (daclatasvir tablets) + pegylated interferon + ribavirin [unapproved regimen] were studied.

Guidelines

The American Association for the Study of Liver Diseases (AASLD)/ Infectious Diseases Society of America (IDSA) recommendations related to Mavyret are summarized below in Table 3. For the most up-

to-date information always refer to the guidelines. In treatment-naïve adults without cirrhosis the recommended regimens are Mavyret for 8 weeks or Epclusa for 12 weeks. In treatment-naïve adults with compensated cirrhosis, the recommended regimens are Mavyret for 8 weeks (genotypes 1 through 6) or Epclusa for 12 weeks (genotypes 1, 2, 4, 5, or 6; patients with genotype 3 require baseline NS5A resistance-associated substitution testing and those without Y93H can be treated with 12 weeks of Epclusa). Additional genotype-specific and/or special circumstance-specific recommendations are also provided (Table 3).

Table 3. AASLD Recommendations for Mavyret.[7]

DAA	Duration	FDA Approved (Y/N)	AASLD Level of Evidence
Chronic HCV – Treatment-Naïve – Recommended			
Genotype 1, 2, 3, 4, 5, 6 – No Cirrhosis			
Mavyret	8 weeks	Y	Class I, Level A
Genotype 1, 3 Compensated Cirrhosis			
Mavyret	8 weeks	Y	Class I, Level B
Genotype 2, 4, 5, 6 Compensated Cirrhosis			
Mavyret	12 weeks	Y	Class I, Level B
Chronic HCV – Treatment-Experienced			
Peglyated Interferon/Ribavirin			
Genotype 1, 2, 4, 5, 6 – Recommended			
Mavyret	8 weeks (no cirrhosis) 12 weeks (compensated cirrhosis)	Y Y	Class I, Level A (Class IIa, Level B for genotype 5) Class I, Level B (Class IIa, Level B for genotype 4)
Genotype 3 – Alternative			
Mavyret	16 weeks (± compensated cirrhosis)	Y	Class IIa, Level B
NS3/4A (Incivek, Victrelis, Olysio + Pegylated Interferon/Ribavirin			
Genotype 1 – Recommended			
Mavyret	12 weeks (± compensated cirrhosis)	Y	Class IIa, Level B
Non-NS5A Sovaldi-Containing Regimen			
Genotype 1 – Alternative			
Mavyret	16 weeks (± compensated cirrhosis NOT NS3/4A experienced)	Y	Class IIa, Level B
Sovaldi + WBR			
Genotype 2 – Recommended			
Mavyret	12 weeks (± compensated cirrhosis)	Y	Class IIb, Level B
Genotype 3 – Recommended			
Mavyret	16 weeks (± compensated cirrhosis)	N	Class IIb, Level B
Recurrent HCV Post-Liver Transplant – Treatment-Naïve or Treatment-Experienced			
Genotype 1, 2, 3, 4, 5, 6 – Recommended			
Mavyret	12 weeks (± compensated cirrhosis)	N	Class I, Level B (no cirrhosis) Class 1, Level C (compensated cirrhosis)
Organ Recipients from HCV RNA-Positive Donors			
Genotype 1, 2, 3, 4, 5, 6 – Recommended			
Mavyret	12 weeks	N	Class I, Level C
Stage 4 or 5 CKD (eGFR < 30 mL/min) or ESRD and Chronic HCV			
Genotype 1, 2, 3, 4, 5, 6 – Recommended			
Mavyret	8 to 16 weeks	Y	Class I, Level A

Table 3 (continued). AASLD Recommendations for Mavyret.[7]

DAA	Duration	FDA Approved (Y/N)	AASLD Level of Evidence
Kidney Transplant with HCV Treatment-Naïve or –Experienced ± Compensated Cirrhosis			
Genotype 1, 2, 3, 4, 5, 6 – Recommended			
Mavyret	12 weeks	Y	Class I, Level A (no cirrhosis) Class IIa, Level C (compensated cirrhosis)
Pediatric Patients			
Genotype 1, 2, 3, 4, 5, 6 – Treatment-Naïve Adolescents ≥ 12 years or ≥ 45 kg, ± Compensated Cirrhosis – Recommended			
Mavyret	8 weeks	Y	Class I, Level B
Genotype 1, 2, 3, 4, 5, 6 – Treatment-Experienced Adolescents ≥ 12 years or ≥ 45 kg, ± Compensated Cirrhosis – Recommended			
Mavyret	8 weeks (GT 1, 2, 4, 5, or 6 without cirrhosis)	Y	Class I, Level B
	12 weeks (GT 1, 2, 4, 5, or 6 compensated cirrhosis)	Y	Class I Level B
	16 weeks (GT 3 ± compensated cirrhosis)	Y	Class I, Level B
	16 weeks (GT1 ± compensated cirrhosis)	Y	Class I, Level B
	12 weeks (GT1 without cirrhosis)	Y	Class I, Level B

AASLD – American Association for the Study of Liver Diseases; DAA – Direct-acting antiviral; Y – Yes; N – No; HCV – Hepatitis C virus; WBR – Weight-based ribavirin; CKD – Chronic kidney disease; ESKD – End-stage kidney disease.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Mavyret. See criteria for approval durations. Because of the specialized skills required for evaluation and diagnosis of patients treated with Mavyret as well as the monitoring required for adverse events and efficacy, approval requires Mavyret to be prescribed by or in consultation with a physician who specialized in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Mavyret is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Chronic Hepatitis C Virus (HCV) Genotype 1, 2, 3, 4, 5, or 6, Treatment-Naïve.** Approve for 8 weeks if the patient meets the following criteria (A, B, and C):
   - **A)** Patient is ≥ 12 years of age OR ≥ 45 kg; AND
   - **B)** Patient is HCV treatment-naïve (the patient has not previously received treatment for their chronic HCV infection); AND
   - **C)** Mavyret is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician.

2. **Chronic Hepatitis C Virus (HCV), Genotype 1, Treatment-Experienced.** Approve for the duration noted if the patient meets the following criteria (A, B, and C):
   - **A)** Patient is ≥ 12 years of age OR ≥ 45 kg; AND
   - **B)** Patient meets ONE of the following conditions (i, ii, iii, or iv):

     NS5A-Experienced, NS3/4-Naïve

     - **i.** Approve for 16 weeks if the patient meets both of the following criteria (a, b, and c):
       - **a)** The patient does not have cirrhosis or has compensated cirrhosis (Child-Pugh A); AND
       - **b)** Patient had a prior null response, prior partial response, or had relapse after prior treatment with one of the following NS5A-inhibitor containing products: Daklinza (daclatasvir

tablets), Epclusa (sofosbuvir/velpatasvir brand or generic), Harvoni (ledipasvir/sofosbuvir tablets/oral pellets; brand or generic); AND

c) Patient has not previously been treated with one of the following NS3/4A inhibitor or NS3/4A inhibitor-containing products: Olysio (simeprevir capsules), Victrelis (boceprevir capsules), or Incivek (telaprevir tablets), Technivie (ombitasvir/paritaprevir/ritonavir tablets), Viekira Pak (ombitasvir/paritaprevir/ritonavir tablets; dasabuvir tablets, co-packaged), Viekira XR (dasabuvir/ombitasvir/paritaprevir/ritonavir extended-release tablets), Vosevi (sofosbuvir/velpatasvir/voxilaprevir); or Zepatier (elbasvir/grazoprevir tablets); OR

NS3/4-Experienced, NS5A-Naïve

ii. Approve for 12 weeks if the patient meets both of the following criteria (a, b, and c):

a) Patient does not have cirrhosis or has compensated cirrhosis (Child-Pugh A).

b) Patient has not previously been treated with one of the following NS5A-inhibitor-containing products: Daklinza (daclatasvir tablets), Epclusa (sofosbuvir/velpatasvir brand or generic), Harvoni (ledipasvir/sofosbuvir tablets/oral pellets; brand or generic), Technivie (ombitasvir/paritaprevir/ritonavir tablets), Viekira Pak (ombitasvir/paritaprevir/ritonavir tablets; dasabuvir tablets, co-packaged), Viekira XR (dasabuvir/ombitasvir/paritaprevir/ritonavir extended-release tablets), Vosevi (sofosbuvir/velpatasvir/voxilaprevir), or Zepatier (elbasvir/grazoprevir tablets); AND

c) Patient had a prior null response, prior partial response, or had relapse after prior treatment with one of the following NS3/4A inhibitor or NS3/4A inhibitor-containing products: Olysio (simeprevir capsules), Victrelis (boceprevir capsules), or Incivek (telaprevir tablets); OR

Pegylated Interferon/Interferon, Ribavirin, Sovaldi-Experienced

iii. Approve for 8 weeks if the patient meets both of the following criteria (a and b):

a) Patient does not have cirrhosis; AND

b) Patient had a prior null response, prior partial response, or had relapse after prior treatment with one of the following regimens: interferon ± ribavirin, pegylated interferon ± ribavirin, Sovaldi (sofosbuvir tablets/oral pellets) + ribavirin, Sovaldi + pegylated interferon + ribavirin; AND

iv. Approve for 12 weeks if the patient meets both of the following criteria (a and b):

a) Patient has compensated cirrhosis (Child-Pugh A); AND

b) Patient had a prior null response, prior partial response, or had relapse after prior treatment with one of the following regimens: interferon ± ribavirin, pegylated interferon ± ribavirin, Sovaldi (sofosbuvir tablets/oral pellets) + ribavirin, Sovaldi + pegylated interferon + ribavirin; AND

C) Mavyret is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician.

3. Chronic Hepatitis C Virus (HCV), Genotype 2, 4, 5, or 6, Treatment-Experienced. Approve for the duration noted if the patient meets the following criteria (A, B, C, and D):

A) Patient is ≥ 12 years of age OR ≥ 45 kg; AND

B) Patient meets ONE of the following (i or ii):

i. Approve for 8 weeks if the patient meets both of the following criteria (a and b):

a) Patient does not have cirrhosis; AND

b) Patient had a prior null response, prior partial response, or had relapse after prior treatment with one of the following regimens: interferon ± ribavirin, pegylated interferon ± ribavirin, Sovaldi (sofosbuvir tablets/oral pellets)+ ribavirin, Sovaldi + pegylated interferon + ribavirin; OR

ii. Approve for 12 weeks if the patient meets both of the following criteria a and b):

a) Patient has compensated cirrhosis (Child-Pugh A); AND

b) Patient had a prior null response, prior partial response, or had relapse after prior treatment with one of the following regimens: interferon ± ribavirin, pegylated interferon ± ribavirin, Sovaldi (sofosbuvir tablets/oral pellets) + ribavirin, Sovaldi + pegylated interferon + ribavirin; AND

C) Mavyret is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician.

4. Chronic Hepatitis C Virus (HCV), Genotype 3, Treatment-Experienced. Approve for 16 weeks if the patient meets the following criteria (A, B, C, and D):

A) Patient is 12 years of age OR ≥ 45 kg; AND

B) Patient does not have cirrhosis or has compensated cirrhosis (Child-Pugh A); AND

C) Patient had a prior null response, prior partial response, or had relapse after prior treatment with one of the following regimens: interferon ± ribavirin, pegylated interferon ± ribavirin, Sovaldi (sofosbuvir tablets/oral pellets) + ribavirin, Sovaldi + pegylated interferon + ribavirin; AND

D) Mavyret is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician.

5. Hepatitis C Virus (HCV) Kidney or Liver Transplant Recipients, Genotype 1, 2, 3, 4, 5, OR 6. Approve for the duration noted if the patient meets all of the following criteria (A, B, C and D):

A) Patient is 12 years of age OR ≥ 45 kg; AND

B) Patient is a kidney or liver transplant recipient with hepatitis C virus (HCV); AND

C) Patient meets one of the following conditions (i, ii, or iii):

i. Patient has genotype 2, 4, 5, or 6 HCV: Approve for **12 weeks**;

ii. Patient has genotype 1 HCV: Approve for the duration below (a or b):

NS5A-Experienced, NS3/4-Naïve

a) Approve for 16 weeks if the patient meets both of the following criteria (1 and 2):

(1) Patient had a prior null response, prior partial response, or had relapse after prior treatment with one of the following NS5A-inhibitor containing products: Daklinza (daclatasvir tablets), Epclusa (sofosbuvir/velpatasvir brand or generic) Harvoni (ledipasvir/sofosbuvir tablets/oral pellets; brand or generic); AND

(2) Patient has not previously been treated with one of the following NS3/4A inhibitor or NS3/4A inhibitor-containing products: Olysio (simeprevir capsules), Victrelis (boceprevir capsules), or Incivek (telaprevir tablets), Technivie (ombitasvir/paritaprevir/ritonavir tablets), Viekira Pak (ombitasvir/paritaprevir/ritonavir tablets; dasabuvir tablets, co-packaged), Viekira XR (dasabuvir/ombitasvir/paritaprevir/ritonavir extended-release tablets), Vosevi (sofosbuvir/velpatasvir/voxilaprevir); or Zepatier (elbasvir/grazoprevir tablets). OR

b) Approve for 12 weeks for all other patients with genotype 1 HCV; OR

iii. Patient has genotype 3 HCV: Approve for the duration below (a or b):

a) Approve for 16 weeks if the patient meets the following criteria (1):

(1) Patient had a prior null response, prior partial response, or had relapse after prior treatment with one of the following regimens: interferon ± ribavirin, pegylated interferon ± ribavirin, Sovaldi (sofosbuvir tablets/oral pellets) + ribavirin, Sovaldi + pegylated interferon + ribavirin**;** OR

b) Approve for 12 weeks for all other patients with genotype chronic HCV; AND

D) Mavyret is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician.

Other Uses with Supportive Evidence

6. **Recurrent Hepatitis C Virus (HCV) Post-Liver Transplantation, Genotype 1, 2, 3, 4, 5, OR 6.** Approve for 12 weeks in patients who meet the following criteria (A, B, and C):
   A) Patient is ≥ 12 years of age OR ≥ 45 kg; AND
   B) Patient has recurrent hepatitis C virus (HCV) after a liver transplantation; AND
   C) Mavyret is prescribed by or in consultation with one of the following prescribers who is affiliated with a transplant center: a gastroenterologist, hepatologist, infectious diseases physician, or liver transplant physician.

7. **Patient Has Been Started on Mavyret.** Approve for an indication or condition addressed as an approval in the Recommended Authorization Criteria section (FDA-Approved Indications or Other Uses with Supportive Evidence). Approve the duration described above to complete a course therapy (e.g., a patient who should receive 12 weeks, and has received 3 weeks should be approved for 9 weeks to complete their 12-week course).

CONDITIONS NOT RECOMMENDED FOR APPROVAL
Coverage of Mavyret is not recommended in the following situations:

1. **Hepatitis C Virus (HCV) Child-Pugh Class B or C Liver Disease (Moderate or Severe Hepatic Impairment).** Mavyret is contraindicated in patients with moderate or severe hepatic impairment (Child-Pugh Class B or C).

2. **Hepatitis C Virus (HCV) [any genotype], Combination with Any Other Direct-Acting Antivirals**. Mavyret provides a complete antiviral regimen.

3. **Life Expectancy Less Than 12 Months Due to Non-Liver Related Comorbidities.** Patients with a limited life expectancy that cannot be remediated by HCV treatment, liver transplantation, or another directed therapy do not require antiviral treatment.[2] Patients with a short life expectancy owing to liver disease should be managed in consultation with an expert. Little evidence exists to support initiation of HCV treatment in patients with a limited life expectancy (< 12 months) owing to non-liver-related comorbid conditions. For these patients, the benefits of HCV treatment are unlikely to be realized and palliative care strategies should take precedence.

4. **Pediatric Patients (Age < 12 Years or < 45 kg).** The safety and efficacy of Mavyret have not been established in pediatric patients < 12 years of age or < 45 kg.[1]

5. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Mavyret™ tablets [prescribing information]. North Chicago, IL: AbbVie; May 2020.
2. American Association for the Study of Liver Diseases and the Infectious Diseases Society of America. Testing, managing, and treating hepatitis C. Available at: http://www.hcvguidelines.org. Updated November 6, 2019. Accessed on August 11, 2020.