

Clinical Policy: Glecaprevir/Pibrentasvir (Mavyret)

Reference Number: IL.ERX.SPA.215

Effective Date: 06.01.21

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Line of Business: Illinois Medicaid

[Revision Log](#)

See **Important Reminder** at the end of this policy for important regulatory and legal information.

Description

Glecaprevir and pibrentasvir (Mavyret[®]) are a fixed-dose combination of glecaprevir, a hepatitis C virus (HCV) NS3/4A protease inhibitor, and pibrentasvir, an HCV NS5A inhibitor.

FDA Approved Indication(s)

Mavyret is indicated for the treatment of adults and pediatric patients 3 years and older with:

- Chronic HCV genotype 1, 2, 3, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis (Child-Pugh A)
- 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

* In clinical trials, prior NS5A inhibitor experience included ledipasvir and sofosbuvir or daclatasvir with pegylated interferon and ribavirin.

** In clinical trials, prior NS3/4A protease inhibitor experience included regimens containing simeprevir and sofosbuvir, or simeprevir, boceprevir, or telaprevir with pegylated interferon and ribavirin.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions[™] that Mavyret is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Chronic Hepatitis C Infection (must meet all):

1. Diagnosis of chronic HCV infection as evidenced by detectable HCV RNA levels by quantitative assay in the last 6 months;
2. Confirmed HCV genotype is one of the following (a, b, c, or d):
 - a. For treatment-naïve members: genotypes 1, 2, 3, 4, 5, or 6;
 - b. For members treatment-experienced with interferon (IFN)/pegylated-interferon (pegIFN), ribavirin (RBV), and/or sofosbuvir only: genotypes 1, 2, 3, 4, 5, or 6;
 - c. For members treatment-experienced with either an NS5A inhibitor or an NS3/4A protease inhibitor: genotype 1 (see *Appendix D*);
 - d. For Vosevi-experienced members, member meets both of the following (i and ii):
 - i. Member has genotype 1, 2, 3, 4, 5, or 6;
 - ii. Member must use Vosevi in combination with weight-based RBV, unless contraindicated or clinically significant adverse effects are experienced;

*Chart note documentation and copies of lab results are required

3. Prescribed by or in consultation with a gastroenterologist, hepatologist, or infectious disease specialist, or provider who has expertise in treating HCV based on a certified training program (see *Appendix F*);
4. Age \geq 3 years;
5. If cirrhosis is present, confirmation of Child-Pugh A status;
6. Life expectancy \geq 12 months with HCV treatment;

7. Member is not treatment-experienced with both NS3/4A protease inhibitor AND NS5A inhibitors, such as combination therapies including Technivie™, Viekira®, and Zepatier®;
8. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (see *Section V Dosage and Administration for reference*);
9. Dose does not exceed one of the following (a, b, c, or d):
 - a. Adult and pediatric members 12 years of age and older or with body weight ≥ 45 kg: glecaprevir 300 mg and pibrentasvir 120 mg (3 tablets) per day;
 - b. Pediatric members 3 years to < 12 years of age with body weight < 20 kg: glecaprevir 150 mg and pibrentasvir 60 mg per day;
 - c. Pediatric members 3 years to < 12 years of age with body weight 20 kg to < 30 kg: glecaprevir 200 mg and pibrentasvir 80 mg per day;
 - d. Pediatric members 3 years to < 12 years of age with body weight 30 kg to < 45 kg: glecaprevir 250 mg and pibrentasvir 100 mg per day.

Approval duration: Up to a total of 16 weeks*

(*Approved duration should be consistent with a regimen in *Section V Dosage and Administration*)

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Chronic Hepatitis C Infection (must meet all):

1. Member meets one of the following (a or b):
 - a. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
 - b. Both of the following (i and ii):
 - i. Documentation supports that member is currently receiving Mavyret for chronic HCV infection and has recently completed at least 40 days of treatment with Mavyret;
 - ii. Confirmed HCV genotype is one of the following (1, 2, 3, or 4):
 - 1) For treatment-naïve members: genotypes 1, 2, 3, 4, 5, or 6;
 - 2) For members treatment-experienced with interferon (IFN)/pegylated-interferon (pegIFN), ribavirin (RBV), and/or sofosbuvir only: genotypes 1, 2, 3, 4, 5, or 6;
 - 3) For members treatment-experienced with either an NS5A inhibitor or an NS3/4A protease inhibitor: genotype 1 (*see Appendix D*);
 - 4) For Vosevi-experienced members: genotypes 1, 2, 3, 4, 5, or 6;
2. Member is responding positively to therapy;
3. Dose does not exceed one of the following (a, b, c, or d):
 - a. Adult and pediatric members 12 years of age and older or with body weight ≥ 45 kg: glecaprevir 300 mg and pibrentasvir 120 mg (3 tablets) per day;
 - b. Pediatric members 3 years to < 12 years of age with body weight < 20 kg: glecaprevir 150 mg and pibrentasvir 60 mg per day;
 - c. Pediatric members 3 years to < 12 years of age with body weight 20 kg to < 30 kg: glecaprevir 200 mg and pibrentasvir 80 mg per day;
 - d. Pediatric members 3 years to < 12 years of age with body weight 30 kg to < 45 kg: glecaprevir 250 mg and pibrentasvir 100 mg per day.

Approval duration: Up to a total of 16 weeks*

(*Approved duration should be consistent with a regimen in *Section V Dosage and Administration*)

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

- A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents;

- B. Treatment-experienced patients with both NS3/4A protease inhibitor AND NS5A inhibitor, such as combination therapies including: Technivie, Viekira, and Zepatier.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AASLD: American Association for the Study of Liver Diseases	IDSA: Infectious Diseases Society of America
FDA: Food and Drug Administration	NS3/4A, NS5A/B: nonstructural protein
HBV: hepatitis B virus	PegIFN: pegylated interferon
HCV: hepatitis C virus	RBV: ribavirin
	RNA: ribonucleic acid

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
 - Patients with severe hepatic impairment (Child-Pugh B or C)
 - Co-administration with atazanavir and rifampin
- Boxed warning(s): risk of hepatitis B virus reactivation in patients coinfecting with HCV and HBV.

Appendix D: Direct-Acting Antivirals (DAAs) for Treatment of HCV Infection

Brand Name	Drug Class				
	NS5A Inhibitor	Nucleotide Analog NS5B Polymerase Inhibitor	Non-Nucleoside NS5B Polymerase Inhibitor	NS3/4A Protease Inhibitor (PI)**	CYP3A Inhibitor
Epclusa*	Velpatasvir	Sofosbuvir			
Harvoni*	Ledipasvir	Sofosbuvir			
Mavyret*	Pibrentasvir			Glecaprevir	
Sovaldi		Sofosbuvir			
Viekira PAK*	Ombitasvir		Dasabuvir	Paritaprevir	Ritonavir
Vosevi*	Velpatasvir	Sofosbuvir		Voxilaprevir	
Zepatier*	Elbasvir			Grazoprevir	

*Combination drugs

Appendix E: General Information

- Hepatitis B Virus Reactivation (HBV) is a Black Box Warning for all direct-acting antiviral drugs for the treatment of HCV. HBV reactivation has been reported when treating HCV for patients co-infected with HBV, leading to fulminant hepatitis, hepatic failure, and death, in some cases. Patients should be monitored for HBV reactivation and hepatitis flare during HCV treatment and post-treatment follow-up, with treatment of HBV infection as clinically indicated.
- Due to higher rates of virologic failure and treatment-emergent drug resistance, the data do not support labeling for treatment of HCV genotype 1 infected patients who are both NS3/4A PI and NS5A inhibitor-experienced.

Appendix F: Healthcare Provider HCV Training

Acceptable HCV training programs and/or online courses include, but are not limited to the following:

- Hepatitis C online course (<https://www.hepatitisc.uw.edu/>): University of Washington is funded by the Division of Viral Hepatitis to develop a comprehensive, online self-study course for medical providers on diagnosis, monitoring, and management of hepatitis C virus infection. Free CME and CNE credit available.
- Fundamentals of Liver Disease (<https://liverlearning.aasld.org/fundamentals-of-liver-disease/>): The AASLD, in collaboration with ECHO, the American College of Physicians (ACP), CDC, and the

Department of Veterans Affairs, has developed Fundamentals of Liver Disease, a free, online CME course to improve providers' knowledge and clinical skills in hepatology.

- Clinical Care Options: <http://www.clinicaloptions.com/hepatitis.aspx>
- CDC training resources: <https://www.cdc.gov/hepatitis/resources/professionals/trainingresources.htm>

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose	Reference
Genotypes 1-6: Treatment-naive	Without cirrhosis or with compensated cirrhosis: Three tablets PO QD for 8 weeks	Adults/Peds age ≥ 12 years or with body weight ≥ 45 kg: glecaprevir 300 mg/pibrentasvir 120 mg (3 tablets) per day;	FDA-approved labeling
Genotypes 1, 2, 4, 5, or 6: Treatment-experienced with IFN/pegIFN + RBV and/or sofosbuvir	Without cirrhosis: Three tablets PO QD for 8 weeks With compensated cirrhosis: Three tablets PO QD for 12 weeks	Peds age 3 years to < 12 years of age with body weight < 20 kg: glecaprevir 150 mg/pibrentasvir 60 mg per day;	
Genotypes 3: Treatment-experienced with IFN/pegIFN + RBV and/or sofosbuvir	Without cirrhosis or with compensated cirrhosis: Three tablets PO QD for 16 weeks	Peds age 3 years to < 12 years of age with body weight 20 kg to < 30 kg: glecaprevir 200 mg/pibrentasvir 80 mg per day;	
Genotype 1: Treatment-experienced with NS5A inhibitor* without prior NS3/4A protease inhibitor*	Without cirrhosis or with compensated cirrhosis: Three tablets PO QD for 16 weeks	Peds age 3 years to < 12 years of age with body weight 30 kg to < 45 kg: glecaprevir 250 mg/pibrentasvir 100 mg per day	
Genotype 1: Treatment-experienced with NS3/4A protease inhibitor* without prior NS5A inhibitor*	Without cirrhosis or with compensated cirrhosis: Three tablets PO QD for 12 weeks		
Genotype 1-6: Treatment-naïve or treatment-experienced, post-liver or kidney transplantation without cirrhosis or with compensated cirrhosis	Three tablets PO QD for 12 weeks (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 IFN/pegIFN, RBV and/or sofosbuvir treatment-experienced)*		

Indication	Dosing Regimen	Maximum Dose	Reference
Genotypes 1-6: Patients with prior sofosbuvir/velpatasvir/voxilaprevir treatment failure	With or without compensated cirrhosis: Mavyret 3 tablets PO QD + Sovaldi 400 mg + weight-based RBV for 16 weeks	Three tablets (glecaprevir 300 mg/ pibrentasvir 120 mg) per day	AASLD-IDSA (updated March 2021)

AASLD/IDSA treatment guidelines for chronic hepatitis C infection are updated at irregular intervals; refer to the most updated AASLD/IDSA guideline for most accurate treatment regimen.

* See appendix D

VI. Product Availability

- Tablets: glecaprevir 100 mg with pibrentasvir 40 mg
- Oral pellet: glecaprevir 50 mg and pibrentasvir 20 mg

VII. References

1. Mavyret Prescribing Information. North Chicago, IL: AbbVie Inc.; June 2021. Available at: www.mavyret.com. Accessed July 12, 2021.
2. American Association for the Study of Liver Diseases/ Infectious Disease Society of America (AASLD-IDSA). HCV guidance: recommendations for testing, managing, and treating hepatitis C. Last updated March 12, 2021. Available at: <https://www.hcvguidelines.org/>. Accessed April 15, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	04.27.21	05.21
3Q 2021 annual review: removed criterion for sobriety documentation as AASLD recommends to treat all patients with HCV except those with short life expectancy; updated section V dosing tables; RT4: updated criteria for Mavyret pediatric age expansion to 3 years and older along with pediatric dosing and new oral pellet dosage formulation; references reviewed and updated.	07.16.21	08.21

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

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