

Clinical Policy: Glecaprevir/Pibrentasvir (Mavyret)

Reference Number: CP.PHAR.348

Effective Date: 09.17

Last Review Date: 08.23

Line of Business: 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 adult 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.

It is the policy of health plans affiliated with Centene Corporation® that Mavyret is **medically necessary** when the following criteria are met:

1. Initial Approval Criteria**A. Chronic Hepatitis C Infection (must meet all):**

1. Diagnosis of chronic HCV infection as evidenced by detectable serum HCV RNA levels by quantitative assay in the last 6 months;
2. Member meets one of the following (a or b):
 - a. Member is treatment-naïve and has either compensated cirrhosis or no cirrhosis (i.e., eligible for simplified treatment regimen);
 - b. Confirmed HCV genotype is one of the following (i, ii, iii, or iv):*
 - i. For treatment-naïve members: genotypes 1, 2, 3, 4, 5, or 6;
 - ii. For members treatment-experienced with interferon (IFN)/pegylated-interferon (pegIFN), ribavirin (RBV), and/or sofosbuvir only: genotypes 1, 2, 3, 4, 5, or 6;
 - iii. For members treatment-experienced with either an NS5A inhibitor or an NS3/4A protease inhibitor: genotype 1 (*see Appendix D*);
 - iv. For Vosevi®- or Mavyret-experienced members: genotype 1, 2, 3, 4, 5, or 6;

**Chart note documentation and copies of lab results are required*

3. If cirrhosis is present, confirmation of Child-Pugh A status;
4. Age \geq 3 years;
5. Member is not treatment-experienced with both NS3/4A protease inhibitor AND NS5A inhibitors, such as combination therapies including Technivie[™], Viekira[™], and Zepatier[®];
6. Life expectancy \geq 12 months with HCV treatment;
7. Prescribed regimen is consistent with an FDA or AASLD-IDSAs recommended regimen (*see Section V Dosage and Administration for reference*);
8. 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 \geq 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 (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
 - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
 - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Member meets one of the following (a, b, or c):
 - a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
 - b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);

- c. 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 IFN/pegIFN, 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 E*);
 - 4) For Vosevi-experienced members: genotype 1, 2, 3, 4, 5, or 6;
2. Member is not treatment-experienced with both NS3/4A protease inhibitor AND NS5A inhibitors, such as combination therapies including Technivie, Viekira, and Zepatier;
3. Member is responding positively to therapy;
4. 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 \geq 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 (must meet 1 or 2):

1. This drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
 - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
 - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

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 policies – CP.PMN.53 for Medicaid or evidence of coverage documents;
- B. HCV in treatment-experienced members 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
HIV: human immunodeficiency virus	RNA: ribonucleic acid

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

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

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

Brand Name	Drug Class				
	NS5A Inhibitor	Nucleotide Analog NS5B Polymerase Inhibitor	Non-Nucleoside NS5B Palm 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

- HBV reactivation 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.
- Child-Pugh Score:

	1 Point	2 Points	3 Points
Bilirubin	Less than 2 mg/dL Less than 34 umol/L	2-3 mg/dL 34-50 umol/L	Over 3 mg/dL Over 50 umol/L
Albumin	Over 3.5 g/dL Over 35 g/L	2.8-3.5 g/dL 28-35 g/L	Less than 2.8 g/dL Less than 28 g/L
INR	Less than 1.7	1.7 - 2.2	Over 2.2
Ascites	None	Mild / medically controlled	Moderate-severe / poorly controlled
Encephalopathy	None	Mild / medically controlled Grade I-II	Moderate-severe / poorly controlled. Grade III-IV

Child-Pugh class is determined by the total number of points: A = 5-6 points; B = 7-9 points; C = 10-15 points

- AASLD-IDSAsimplified treatment recommendations: In their October 2022 HCV guidance, AASLD-IDSAsimplified treatment recommendations to recommend two simplified regimens for adults with chronic hepatitis C (*any genotype*) who do not have cirrhosis and have not previously received hepatitis C treatment: either Mavyret x8 weeks or Epclusa x12 weeks. Additionally, for adults with chronic hepatitis C (*any genotype*) who have not previously received hepatitis C treatment and either have compensated cirrhosis or do not have cirrhosis: Mavyret x8 weeks is a recommended regimen. (Epclusa x12 weeks is also an option but would require genotype testing in the compensated cirrhosis setting). With the advent of pangenotypic HCV treatment regimens, HCV genotyping is no longer required prior to treatment initiation for all individuals. In those with evidence of cirrhosis and/or past unsuccessful HCV treatment, treatment regimens may differ by genotype and thus pretreatment genotyping is recommended. For noncirrhotic treatment-naive patients, although genotyping may impact the preferred treatment approach, it is not required if a pangenotypic regimen is used.

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	FDA-approved labeling

Indication	Dosing Regimen	Maximum Dose	Reference
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	300 mg/pibrentasvir 120 mg (3 tablets) per day; Peds age 3 years to < 12 years of age with body weight < 20 kg: glecaprevir 150 mg/pibrentasvir 60 mg per day;	
Genotype 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)		
Genotypes 1-6: Patients with prior sofosbuvir/velpatasvir/voxilaprevir or glecaprevir/pibrentasvir 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 October 2022)

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.

** In Mavyret clinical trials, subjects were treated with prior regimens containing ledipasvir and sofosbuvir or daclatasvir with (peg)interferon and RBV*

† In Mavyret clinical trials, subjects were treated with prior regimens containing simeprevir and sofosbuvir, or simeprevir, boceprevir, or telaprevir with (peg)interferon and RBV.

VI. Product Availability

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

VII. References

1. Mavyret Prescribing Information. North Chicago, IL: AbbVie Inc.; September 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/209394s014,215110s0011bl.pdf. Accessed April 21, 2023.
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 October 24, 2022. Available at: <https://www.hcvguidelines.org/>. Accessed May 5, 2023.
3. CDC. Hepatitis C Q&As for health professionals. Last updated August 7, 2020. Available at: <https://www.cdc.gov/hepatitis/hcv/hcvfaq.htm>. Accessed May 5, 2023.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2019 annual review: updated age \geq 12 or weight \geq 45 kg to be consistent with updated FDA approved indication; removed documented sobriety from alcohol and illicit IV drugs for \geq 6 months prior to starting therapy; added missing criterion for requirement against treatment-experience with both NS3/4A protease inhibitor AND NS5A inhibitors; references reviewed and updated.	06.26.19	08.19
RT4: updated dosing recommendations to 8 weeks total duration of therapy for treatment naive HCV with compensated cirrhosis across all genotypes (1-6).	10.03.19	
Added new prescriber requirement to include a “provider who has expertise in treating HCV based on a certified training program”; Appendix F (Healthcare Provider HCV Training) added.	11.07.19	02.20
3Q 2020 annual review: added Mavyret + Sovaldi + RBV preference for Vosevi treatment failures per SDC preferencing and per updated AASLD/IDSA HCV guideline; references reviewed and updated.	05.20.20	08.20
3Q 2021 annual review: no significant changes; updated Section V table with FDA and AASLD recommended regimens; 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.	07.12.21	08.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2022 annual review: no significant changes; clarified confirmed genotype criterion 2 by removing “in combination with sofosbuvir” from Vosevi-experienced members to align with preceding bullets which include genotype and previous treatment experience (approved regimens are listed in section V); references reviewed and updated.	05.05.22	08.22
Template changes applied to other diagnoses/indications and continued therapy section.	09.21.22	
3Q 2023 annual review: added a bypass for HCV genotype documentation if member is treatment-naïve and has either compensated cirrhosis or no cirrhosis (i.e., eligible for AASLD-IDSAsimplified treatment regimen); removed prescriber specialty criterion per Medicaid plan requests; added previous Mavyret experience to initial approval criteria scenarios per AASLD recommended regimens; eliminated adherence program participation criterion due to competitor analysis; references reviewed and updated.	05.31.23	08.23

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan

retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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