# Clinical Policy: Glecaprevir/Pibrentasvir (Mavyret)

Reference Number: GA.PMN.24
Effective Date: 9/17
Last Review Date: 4/2021 Revision Log
Line of Business: Medicaid

**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 12 years and older or weighing at least 45 kg with chronic HCV genotype 1, 2, 3, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis (Child-Pugh A)
- Adult and pediatric patients 12 years and older or weighing at least 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

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

**I. Approval Criteria**
*** Provider must submit documentation (including office chart notes and lab results) supporting that member has met all approval criteria ***

**A. Chronic Hepatitis C Infection** (must meet all)**:**
1. Diagnosis of chronic HCV infection as evidenced by detectable serum HCV RNA (ribonucleic acid) levels by quantitative assay in the last 6 months;
2. Age ≥ 12 years or weight ≥ 45 kg;
3. Confirmed HCV genotype is one of the following (a, b, cor d);
   *Chart note documentation and copies of labs results are required
   a. For treatment-naïve patients: genotypes 1, 2, 3, 4, 5, or 6;
   b. For patients treatment-experienced with interferon (IFN)/pegylated-interferon (pegIFN), ribavirin (RBV), and/or sofosbuvir only: genotypes 1, 2, 3, 4, 5, or 6;
   c. For patients treatment-experienced with either an NS5A inhibitor or an NS3/4A protease inhibitor: genotype 1 (*see Appendix E*)

d. For Vosevi-experienced members in combination with sofosbuvir: genotype 1, 2, 3, 4, 5, or 6;
4. Documentation of the treatment status of the patient (treatment-naïve or treatment-experienced);
5. Documentation of cirrhosis status of the patient (no cirrhosis, compensated cirrhosis, or decompensated cirrhosis);
6. Life expectancy ≥ 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. If cirrhosis is present, confirmation of Child-Pugh A status;
10. Member is hepatitis B virus (HBV) negative, or if positive, documentation that concurrent HBV infection is being treated (e.g., tenofovir alafenamide, adefovir, entecavir), unless contraindicated or clinically significant adverse effects are experienced (*see Appendix E*);
11. Dose does not exceed glecaprevir 300 mg and pibrentasvir 120 mg (3 tablets) per day.

**Approval duration: up to a total of 16 weeks***
*(*Approved duration should be consistent with a regimen in Appendix D FDA approved dosages and Treatment Duration)*

**B. Other diagnoses/indications:** Refer to CP.PHAR.53 – No Coverage Criteria/Off-Label Use Policy if diagnosis is NOT listed specifically in section I.

## II. Appendices/General Information

*Appendix A: Abbreviation/Acronym Key*

AASLD: American Association for the Study of Liver Diseases
APRI: AST to platelet ratio
CTP: Child Turcotte Pugh
CrCl: creatinine clearance
FDA: Food and Drug Administration
FIB-4: Fibrosis-4 index
HCC: hepatocellular carcinoma
HCV: hepatitis C virus
IDSA: Infectious Diseases Society of America
MRE: magnetic resonance elastography
NS3/4A, NS5A/B: nonstructural protein
Peg-IFN: pegylated interferon
PI: protease inhibitor
RBV: ribavirin
RNA: ribonucleic acid

*Appendix B: Therapeutic Alternatives*
Not applicable

*Appendix C: Contraindications/Boxed Warnings*

- Contraindications
  - Patients with moderate or severe hepatic impairment (Child-Pugh B or C)
  - Co-administration with atazanavir or rifampin
- Boxed warning(s): risk of hepatitis B virus reactivation in patients coinfected 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 |
| Daklinza | Daclatasvir | | | | |
| Epclusa* | Velpatasvir | Sofosbuvir | | | |
| Harvoni* | Ledipasvir | Sofosbuvir | | | |
| Mavyret* | Pibrentasvir | | | Glecaprevir | |
| Olysio‡ | | | | Simeprevir | |
| Sovaldi | | Sofosbuvir | | | |
| Technivie*‡ | Ombitasvir | | | Paritaprevir | Ritonavir |
| Viekira /PAK* | Ombitasvir | | Dasabuvir | Paritaprevir | Ritonavir |
| Vosevi* | Velpatasvir | Sofosbuvir | | Voxilaprevir | |
| Zepatier* | Elbasvir | | | Grazoprevir | |

*Combination drugs
‡ *Olysio and Technivie are no longer commercially available.*

*Appendix E: General Information*

- Hepatitis B Virus (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<br>Less than 34 umol/L | 2-3 mg/dL<br>34-50 umol/L | Over 3 mg/dL<br>Over 50 umol/L |
| Albumin | Over 3.5 g/dL<br>Over 35 g/L | 2.8-3.5 g/dL<br>28-35 g/L | Less than 2.8 g/dL<br>Less than 28 g/L |
| INR | Less than 1.7 | 1.7 - 2.2 | Over 2.2 |

| | 1 Point | 2 Points | 3 Points |
|---|---|---|---|
| Ascites | None | Mild / medically controlled | Moderate-severe / poorly controlled |
| Encephalopathy | None | Mild / medically controlled<br>Grade I-II | Moderate-severe / poorly controlled.<br>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*

## III. 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 | Three tablets (glecaprevir 300 mg/pibrentasvir 120 mg) per day | 1) FDA-approved labeling<br>2) AASLD-IDSA (updated November 2019) |
| Genotypes 1, 2, 4, 5, or 6: Treatment-experienced with IFN/pegIFN + RBV | Without cirrhosis: Three tablets PO QD for 8 weeks<br><br>With compensated cirrhosis: Three tablets PO QD for 12 weeks | Three tablets (glecaprevir 300 mg/pibrentasvir 120 mg) per day | 1) FDA-approved labeling<br>2) AASLD-IDSA (updated November 2019) |
| 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<br><br>With compensated cirrhosis: Three tablets PO QD for 12 weeks | Three tablets (glecaprevir 300 mg/pibrentasvir 120 mg) per day | 1) FDA-approved labeling<br>2) AASLD-IDSA (updated November 2019) |
| Genotype 3: Treatment-experienced with IFN/pegIFN + RBV and/or sofosbuvir | Without cirrhosis or with compensated cirrhosis: Three tablets PO QD for 16 weeks | Three tablets (glecaprevir 300 mg/pibrentasvir 120 mg) per day | 1) FDA-approved labeling<br>2) AASLD-IDSA (updated November 2019) |
| 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 | Three tablets (glecaprevir 300 mg/pibrentasvir 120 mg) per day | 1) FDA-approved labeling<br>2) AASLD-IDSA (updated November 2019) |
| 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 | Three tablets (glecaprevir 300 mg/pibrentasvir 120 mg) per day | 1) FDA-approved labeling<br>2) AASLD-IDSA (updated November 2019) |

| Indication | Dosing Regimen | Maximum Dose | Reference |
|---|---|---|---|
| Genotype 1-6: Treatment-naïve or treatment-experienced, post-liver transplantation without cirrhosis or with compensated cirrhosis | Three tablets PO QD for 12 weeks<br><br>(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 PRS treatment-experienced)ǂ | Three tablets (glecaprevir 300 mg/pibrentasvir 120 mg) per day | AASLD-IDSA (updated November 2019) |
| Genotypes 1-6: Patients with prior sofosbuvir/velpatasvir/voxilaprevir treatment failure | With or without compensated cirrhosis:<br><br>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 November 2019) |

*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*
ǂ *PRS: prior treatment experience with regimens containing IFN/pegIFN, RBV, and/or sofosbuvir, but no prior treatment experience with an HCV NS3/4A PI or NS5A inhibitor*

## IV. Product Availability

Tablet: pibrentasvir 40mg with glecaprevir 100mg

## References

1. Mavyret Prescribing Information. North Chicago, IL: AbbVie Inc.; April 2020. Available at: www.mavyret.com. Accessed April 30, 2020.
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3. Platt L, Easterbrook P, Gower E, et al. Prevalence and burden of HCV co-infection in people living with HIV: a global systematic review and meta-analysis. Lancet Infect Dis 2016;16:797-808. http://dx.doi.org/10.1016/
4. Centers for Disease Control and Prevention. HIV and viral hepatitis: fact sheet. June 2017. Available at: https://www.cdc.gov/hiv/pdf/library/factsheets/hiv-viral-hepatitis.pdf. Accessed May 1, 2019.
5. Wolitski R. When it comes to curing hepatitis c, your health care provider may not need to be a specialist. U.S. Department of Health & Human Services. Last updated September 20, 2017. Available at:

https://www.hhs.gov/hepatitis/blog/2017/09/20/study-calls-for-expansion-of-hepatitis-c-treatment.html. Accessed October 30, 2019.
6. CDC. Viral hepatitis: Q&As for health professionals. Last updated July 2, 2019. Available at: https://www.cdc.gov/hepatitis/hcv/hcvfaq.htm. Accessed October 30, 2019.

| Reviews, Revisions, and Approvals | Date | Approval Date |
|---|---|---|
| Policy created | 09/17 | 9/17 |
| Changed current Georgia policy templates to corporate standard templates for drug coverage criteria to meet corporate compliance. Changes/revisions included; new formatting, font size, use of standard policy language for each section of policy, and rearranged order of certain steps in criteria and sections. Removed background sections. Updated general information and contraindication section to be consistent with corporate HCV policies. | 2/21/19 | 2/19 |
| Annual review. Updated age ≥ 12 or weight ≥ 45 kg to be consistent with updated FDA approved indication. Added missing criterion for requirement against treatment-experience with both NS3/4A protease inhibitor AND NS5A inhibitors. | 10/19 | 10/19 |
| RT4: updated dosing recommendations to 8 weeks total duration of therapy for treatment naive HCV with compensated cirrhosis across all genotypes (1-6).Removed Appendix C for Metavir scoring. Removed Mayvret acceptable/unacceptable medical justification and added statement regarding labeling of HCV genotype 1 infected patients in Appendix E. Updated order of all other Appendices. Updated references. | 4/2020 | 4/2020 |
| Added Mavyret + Sovaldi + RBV preference for Vosevi treatment failures per preferencing and per updated AASLD/IDSA HCV guideline; references reviewed and updated. | 7/2020 | 7/2020 |
| Annual review. Added information on drug inclusions for clinical trials in the FDA Approved Indications section. Added moderate hepatic impairment and boxed warning for hepatitis B reactivation to Appendix C: Contraindication. Added a statement regardinig Olysio and Technivie no longer being commercially available to Appendix D. Changed Centene Logo to PSHP Logo. Made minor formatting and typo changes. References reviewed. | 4/2021 | 4/2021 |

**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.