Clinical Policy: Glecaprevir/Pibrentasvir (Mavyret)

Reference Number: GA.PMN.24
Effective Date: 9/17
Last Review Date: 7/2020 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

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 HCV RNA (ribonucleic acid) levels in the last 6 months;
2. Age ≥ 12 years or weight ≥ 45 kg;
3. Confirmed HCV genotype is one of the following (a, b, or c);
   *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
- Patients with severe hepatic impairment (Child-Pugh C)
- Co-administration with atazanavir or rifampin

numerous septa without cirrhosis; F4 = cirrhosis

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			
Olysio				Simeprevir	
Sovaldi		Sofosbuvir			
Technivie*	Ombitasvir			Paritaprevir	Ritonavir
Viekira XR/PAK*	Ombitasvir		Dasabuvir	Paritaprevir	Ritonavir
Zepatier*	Elbasvir			Grazoprevir	

*Combination drugs

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 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

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 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 With compensated cirrhosis: Three tablets PO QD for 12 weeks	Three tablets (glecaprevir 300 mg/pibrentasvir 120 mg) per day	1) FDA-approved labeling 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 With compensated cirrhosis: Three tablets PO QD for 12 weeks	Three tablets (glecaprevir 300 mg/pibrentasvir 120 mg) per day	1) FDA-approved labeling 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 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 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 2) AASLD-IDSA (updated November 2019)
Genotype 1-6: Treatment-naïve or treatment-experienced, post-liver 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	Three tablets (glecaprevir 300 mg/pibrentasvir 120 mg) per day	AASLD-IDSA (updated November 2019)

Indication	Dosing Regimen	Maximum Dose	Reference
	genotype 3-infected patients who are PRS treatment-experienced)[ǂ]		
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 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

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.