Clinical Policy: Glecaprevir/Pibrentasvir (Mavyret)

Reference Number: AZ.CP.PHAR.44
Effective Date: 01.01.18
Last Review Date: 09.18
Line of Business: Arizona 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:

- Patients with chronic HCV genotype 1, 2, 3, 4, 5, or 6 infection without cirrhosis and with compensated cirrhosis (Child-Pugh A).
- Adult patients with 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

Provider must submit documentation (which may include office chart notes and lab results) 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:

I. Initial Approval Criteria

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

1. Diagnosis of chronic HCV infection confirmed by detectable serum HCV RNA by quantitative assay in the last 90 days prior to the date of submission of the request that includes the HCV genotype, viral resistance status (when applicable), hepatic status (Child Pugh Score) and HCV viral load.
2. Confirmed HCV genotype is one of the following (a, b, or c);
   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 D*) AND all of the following:
      i. The member was adherent to Direct Acting Antiviral (DAA) therapy as evidenced by medical records and/or pharmacy claims;
      ii. If prior therapy was discontinued due to adverse effects from the DAA, the medical record shall be provided which

documents these adverse effects and recommendation of discontinuation by treatment provider;

3. Chart note documentation and copies of lab results are required;
4. Prescribed by or in consultation with a gastroenterologist, hepatologist, or infectious disease specialist;
5. Age ≥ 18 years
6. If cirrhosis is present, confirmation of Child-Pugh A status;
7. Patient readiness has been assessed and patient attestation of compliance is submitted and on file in the member's medical record (prescribers shall use the CSPMP as a to aid in the review of compliance);
8. The member agrees to complete the regimen and understands the risks of reinfection and other contributors to liver disease and/or damage, through a signed attestation;
9. The prescribing clinician agrees to maintain HCV RNA levels obtained at 12 and 24-weeks post therapy completion to demonstrate the Sustained Virological Response (SVR);
10. Member has been screened for Hepatitis A and B and shall have received at least one Hepatitis A and at least one Hepatitis B vaccine prior to requesting treatment unless the member demonstrates laboratory evidence of immunity ;
11. For members who have/had a Substance Use Disorder (SUD) in the past 12 months, the member shall be in remission for at least 3 months prior to requesting Hepatitis C treatment and shall be engaged in a SUD treatment program at the time of the prior authorization and over the course of treatment;
12. Dose does not exceed glecaprevir 300 mg and pibrentasvir 120 mg (3 tablets) per day.

Approval duration: 8 to a total of 16 weeks* based on genotype, prior treatment history, and cirrhosis status. *(*Approved duration should be consistent with a regimen in Section V)*

B. Other diagnoses/indications

1. Refer to CP.CPA.09 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. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Mavyret for treatment of chronic HCV infection and has received this medication for at least 30 days;
2. Member is responding positively to therapy (e.g., decreased HCV RNA level, no unacceptable toxicity);
3. 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 Section V)*

B. Other diagnoses/indications

- Refer to CP.CPA.09 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 – CP.CPA.09 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.
C. The member life expectancy is less than 12 months and cannot be remediated by treating the HCV infection, by transplantation or by other directed therapy.
D. The member was non-adherent to the initial DAA treatment regimen as evidenced by medical records and/or pharmacy prescription claims.
E. The treatment is considered an experimental service as defined in R9-22-203. Based on current evidence, this includes more than one retreatment with a DAA and requested retreatment regimens that include more than one DAA.
F. Lost or stolen medications absent of good cause.
G. Fraudulent use of HCV medications.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

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

Appendix B: Required Documentation For Submission of a HCV Prior Authorization Request:

1. HCV treatment history and responses
2. Evidence of Hepatitis A and B vaccination or laboratory evidence of immunity
3. Current medication list
4. Laboratory results for all of the following:
    a. HCV screen
    b. Genotype and current baseline viral load
    c. Total bilirubin
    d. Albumin
    e. INR
    f. CrCl or GFR
    g. LFTs

h. CBC
i. Drug/alcohol screen completed within the past 90 days.

Appendix C: General Information

- Hepatitis B Reactivation is a Black Box Warning for all direct-acting antiviral drugs for the treatment of HCV.
- 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.
- Per the FDA-approved Prescribing Information for Mavyret, "Data on the persistence of glecaprevir and pibrentasvir resistance-associated substitutions are not available…..The long-term clinical impact of the emergence or persistence of virus containing glecaprevir or pibrentasvir resistance-associated substitutions is unknown." Testing for resistance is not required.
- 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

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

Brand Name	Drug Class				
	NS5A Inhibitor	Nucleotide Analog NS5B Polymerase Inhibitor	Non-Nucleoside NS5B Palm Polymerase Inhibitor	NS3/4A Protease Inhibitor (PI)	CYP3A Inhibitor
Viekira XR/Pak*	Ombitasvir		Dasabuvir	Paritaprevir	Ritonavir
Zepatier*	Elbasvir			Grazoprevir	

*Combination drugs

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose	Reference
Genotypes 1, 2, 3, 4, 5, or 6: Treatment-naïve chronic hepatitis C (CHC) infection	Without cirrhosis: 3 tablets PO QD for 8 weeks With compensated cirrhosis or for kidney or liver transplant recipients: 3 tablets PO QD for 12 weeks	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 +/- sofosbuvir CHC infection	Without cirrhosis: 3 tablets PO QD for 8 weeks With compensated cirrhosis: 3 tablets PO QD for 12 weeks	Glecaprevir 300 mg/pibrentasvir 120 mg (3 tablets) per day	FDA-approved labeling
Genotype 3: Treatment-experienced with IFN/pegIFN + RBV +/- sofosbuvir CHC infection	Without cirrhosis or with compensated cirrhosis: 3 tablets PO QD for 16 weeks	Glecaprevir 300 mg/pibrentasvir 120 mg (3 tablets) per day	FDA-approved labeling
Genotype 1: Treatment-experienced with NS5A inhibitor without prior NS3/4A protease inhibitor CHC infection	Without cirrhosis or with compensated cirrhosis: 3 tablets PO QD for 16 weeks	Glecaprevir 300 mg/pibrentasvir 120 mg (3 tablets) per day	FDA-approved labeling
Genotype 1: Treatment-experienced with	Without cirrhosis or with compensated cirrhosis: 3 tablets PO QD for 12 weeks	Glecaprevir 300 mg/pibrentasvir 120 mg (3 tablets)	FDA-approved labeling

NS3/4A protease inhibitor without prior NS5A inhibitor CHC infection		per day	

VI. Product Availability

Tablets: glecaprevir 100 mg and pibrentasvir 40 mg

VII. References

1. Mavyret Prescribing Information. North Chicago, IL: AbbVie Inc.; August 2017. Available at: www.mavyret.com. Accessed August 28, 2018.
2. Institute of Medicine of the National Academies. Beyond Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome Redefining an Illness. Report Brief, February 2015. Available at: https://iom.nationalacademies.org/~/media/Files/Report%20Files/2015/MECFS/MECFS_ReportBrief.pdf. Accessed August 7, 2017.
3. Arizona Health Care Cost Containment System (AHCCCS), AHCCCS Medical Policy Manual (AMPM), Policy 320-N, Hepatitis C Prior Authorization Requirements for Direct Acting Antiviral Medication Treatment, revisions effective 1/1/18.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created. Safety criteria were applied according to the safety guidance discussed at CPAC and endorsed by Centene Medical Affairs. Exception made to require Hep B screening for all patients prior to treatment to ensure that proper risk reduction measures are taking, though this is not specifically addressed in boxed warning.	08.15.17	08.17
Initial approval criteria was clarified from “up to a total of 16 weeks” to “8 to up to a total of 16 weeks” per Corporate P&T feedback.	09.05.17	11.17
Added dosing recommendations for persons with liver or kidney transplants.	08.28.18	

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.

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