Clinical Policy: Glecaprevir/Pibrentasvir (Mavyret)

Reference Number: PA.CP.PHAR.348
Effective Date: 01/18
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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
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 Pennsylvania Health and Wellness ® 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 (ribonucleic acid) levels;
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*);
3. Age ≥ 18 years;
4. If actively abusing alcohol or IV drugs, or has a history of abuse, has documentation of prescriber counseling regarding the risks of alcohol or IV drug abuse and an offer of a referral for substance use disorder treatment.
5. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (*see Section V Dosage and Administration for reference*);
6. Has all of the following:
   a. Documented quantitative HCV RNA at baseline that was tested within the past 3 months.
   b. Dose not have a life expectancy of less than 12 months due to non-liver-related comorbid conditions.

c. Has correct or addressed the causes of non-adherence to a previously prescribed Hepatitis C treatment regimen if the recipient has a history of failed treatment due to non-adherence.
d. Had all potential drug interactions addressed by the prescriber

7. If cirrhosis is present, confirmation of Child-Pugh A status;
8. Has documented completion of
   a. Hepatitis B immunization series or Hepatitis B screening (sAb/sAg and cAb/cAg) AND
   b. If there is detectable HBV DNA, will be treated for Hepatitis B or if negative for hepatitis BsAb, is being vaccinated against Hepatitis B.AND
   c. Has a documented HIV screening (HIV Ag/Ab) and if confirmed positive by HIV-1/HIV-2 differentiation immunoassay: Is being treated for HIV or is not being treated for HIV and the medical record documents the rationale for not being treated
9. Has a documented commitment to adherence with the planned course of treatment
10. 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 Dosage and Administration)*

B. Other diagnoses/indications
1. Refer to PA.CP.PHAR.57 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 Pennsylvania Health and Wellness benefit, or documentation supports that member is currently receiving Mavyret for treatment of chronic HCV infection or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. 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 Dosage and Administration)*

B. Other diagnoses/indications
1. Refer to PA.CP.PHAR.57 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 – PA.CP.PHAR.57 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
DNA: deoxyribonucleic acid
HBeAg: hepatitis B virus envelope antigen
HBV: hepatitis B virus
HCC: hepatocellular carcinoma
HCV: hepatitis C virus
FDA: Food and Drug Administration
FIB-4: Fibrosis-4 index
IDSA: Infectious Diseases Society of America
IFN: interferon
NS3/4A, NS5A/B: nonstructural protein
pegIFN: pegylated interferon
PO: by mouth
QD: once per day
RBV: ribavirin
RNA: ribonucleic acid

Appendix B: General Information

- Hepatitis B Reactivation is a Black Box Warning for all direct-acting antiviral drugs for the treatment of HCV. The provider must provide either:
  - Documentation of absence of concurrent HBV infection as evidenced by laboratory values showing absence of hepatitis B virus envelope antigen (HBeAg) and HBV DNA (deoxyribonucleic acid);
  - Documentation that HBV co-infected patient may not be candidates for therapy as evidenced by one of the following:
    - Absence of HBeAg, HBV DNA less than 2,000 international units/mL, and alanine aminotransferase (ALT) level within 1 to 2 times the upper limit of normal;
    - HBeAg-positive and HBV DNA greater than 1,000,000 international units/mL and ALT level within 1 to 2 times the upper limit of normal;
  - Documentation that concurrent HBV infection is being treated (e.g., tenofovir alafenamide, adefovir, entecavir), unless contraindicated or clinically significant adverse effects are experienced.
- 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 C: 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

V. Dosage and Administration

A. **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.*

Indication	Dosing Regimen	Maximum Dose	Reference
Treatment-naïve Chronic hepatitis C (CHC) infection: Genotypes 1, 2, 3, 4, 5, or 6	Without cirrhosis: 3 tablets by mouth (PO) daily (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 https://www.hcvguidelines.org/
Treatment-experienced with IFN/pegIFN + RBV +/- sofosbuvir CHC infection: Genotypes 1, 2, 4, 5, or 6	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

Indication	Dosing Regimen	Maximum Dose	Reference
	For patients with our without cirrhosis and GT1 and 2 - 12 weeks		
Treatment-experienced with IFN/pegIFN + RBV +/- sofosbuvir CHC infection: Genotype 3	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
Treatment-experienced with NS5A inhibitor without prior NS3/4A protease inhibitor CHC infection: Genotype 1	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
Treatment-experienced with NS3/4A protease inhibitor without prior NS5A inhibitor CHC infection: Genotype 1	Without cirrhosis or with compensated cirrhosis: 3 tablets PO QD for 12 weeks	Glecaprevir 300 mg/pibrentasvir 120 mg (3 tablets) per day	FDA-approved labeling

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 7, 2017.

Reviews, Revisions, and Approvals	Date	Approval Date