RXADVANCE
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Clinical Policy Title:	**glecaprevir/pibrentasvir**
Policy Number:	**RxA.214**
Drug(s) Applied:	**Mavyret™**
Original Policy Date:	**02/07/2020**
Last Review Date:	**09/14/2020**
Line of Business Policy Applies to:	**All lines of business**

Background

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. It 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.

*** In clinical trials, prior treatment experience included regimens containing interferon, pegylated interferon, ribavirin, and/or sofosbuvir, but no prior treatment experience with an HCV NS3/4A protease inhibitor or NS5A inhibitor.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Glecaprevir/Pibrentasvir (Mavyret)	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
	genotypes 1, 2, 4, 5, or 6: treatment-experienced with IFN/pegIFN + RBV	without cirrhosis: three tablets po qd for 8 weeks with compensated	three tablets (glecaprevir 300 mg/ pibrentasvir 120 mg) per day

		cirrhosis: three tablets po qd for 12 weeks	
Glecaprevir/Pibrentasvir (Mavyret)	genotypes 1 or 2: treatment-experienced with sofosbuvir	without cirrhosis or with compensated cirrhosis: three tablets po qd for 12 weeks	three tablets (glecaprevir 300 mg/ pibrentasvir 120 mg) per day
	genotypes 3, 4, 5, or 6: treatment-experienced with sofosbuvir	without cirrhosis or with compensated cirrhosis: three tablets po qd for 12 weeks	three tablets (glecaprevir 300 mg/ pibrentasvir 120 mg) per day
	genotype 3: treatment-experienced with IFN/pegIFN + RBV	without cirrhosis or with compensated cirrhosis: three tablets po qd for 16 weeks	three tablets (glecaprevir 300 mg/ pibrentasvir 120 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	three tablets (glecaprevir 300 mg/ pibrentasvir 120 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	three tablets (glecaprevir 300 mg/ pibrentasvir 120 mg) per day
	genotype 1-6: treatment-naïve or treatment-experienced, post-liver or kidney transplantation with or without 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 PRS treatment- experienced)	three tablets (glecaprevir 300 mg/ pibrentasvir 120 mg) per day

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

Dosage Forms

- Tablets: glecaprevir 100 mg and pibrentasvir 40 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. 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. 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 ;

   *Chart note documentation and copies of lab results are required
3. Prescribed by or in consultation with a gastroenterologist, hepatologist, or infectious disease specialist;
4. Age ≥ 12 years or weight ≥ 45 kg;
5. If cirrhosis is present, confirmation of Child-Pugh A status;
6. Member is not treatment-experienced with both NS3/4A protease inhibitor AND NS5A inhibitors, such as combination therapies including Technivie, Viekira, and Zepatier;
7. Life expectancy ≥ 12 months with HCV treatment;
8. Member agrees to participate in a medication adherence program meeting both of the following components (a and b):
   a. Medication adherence monitored by pharmacy claims data or member report;
   b. Member's risk for non-adherence identified by adherence program or member/prescribing physician follow-up at least every 4 weeks;
9. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (see Section V Dosage and Administration for reference);
10. Dose does not exceed glecaprevir 300 mg and pibrentasvir 120 mg (3 tablets) per day.

Approval Duration

Commercial: 4 months*

Medicaid: 4 months*

(*Approved duration should be consistent with a regimen in Background)

II. Continued Therapy Approval

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy
   b. Must meet 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, or 3);

1) For treatment-naïve members: genotypes 1, 2, 3, 4, 5, or 6;
2) For members treatment-experienced with interferon (IFN)/pegylated- interferon (pegIFN), ribavirin (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*);

2. Member is responding positively to therapy;
3. Dose does not exceed glecaprevir 300 mg and pibrentasvir 120 mg (3 tablets) per day.

Approval Duration

Commercial: 4 months*

Medicaid: 4 months*

(*Approved duration should be consistent with a regimen in Background)

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

AASLD: American Association for the Study of Liver Diseases
FDA: Food and Drug Administration HBV: hepatitis B virus
HCV: hepatitis C virus
HIV: human immunodeficiency virus
IDSA: Infectious Diseases Society of America
NS3/4A, NS5A/B: nonstructural protein
PegIFN: pegylated interferon
RBV: ribavirin
RNA: ribonucleic acid

APPENDIX B: Therapeutic Alternatives

Not applicable

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Patients with severe hepatic impairment (Child-Pugh 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: General Information

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 XR/PAK*	Ombitasvir		Dasabuvir	Paritaprevir	Ritonavir
Vosevi*	Velpatasvir	Sofosbuvir		Voxilaprevir	
Zepatier*	Elbasvir			Grazoprevir	

*Combination drugs

APPENDIX E: General Information

- Hepatitis B Virus Reactivation (HBV) 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

References

1. Mavyret Prescribing Information. North Chicago, IL: AbbVie Inc.; May 2020. Available at: www.mavyret.com. Accessed June 18, 2020.

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 Nov 6, 2019. Available : https://www.hcvguidelines.org/. Accessed June 18, 2020.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Clinical Policy title was updated 2. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 3. Lines of business 'Policy Applies to' was updated to 'All lines of business'. 4. Dosing information updated; added "with compensated cirrhosis" 5. Approval Duration changed from 16 weeks to 4 months (consistency). 6. References reviewed and updated.	06/18/2020	9/14/2020