Clinical Policy: glecaprevir-pibrentasvir (Mavyret)

Reference Number: NM.CP.PPA.01
Effective Date: 1/1/19
Last Review Date: 1/11/23
Revision Log

Description and FDA Approved Indication(s)

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. Mavyret is indicated for the treatment of:

- Treatment naïve adult and pediatric patients 3 years and older with chronic HCV genotype 1, 2, 3, 4, 5, or 6 infection*** without cirrhosis or with compensated cirrhosis (Child-Pugh A)
- Treatment experienced adult and pediatric patients 3 years and older with genotype 1 infection without cirrhosis or with compensated cirrhosis (Child-Pugh A), who previously have been treated with a regimen containing an HCV NS5A inhibitor* or an NS3/4A protease inhibitor**, but not both.
- Treatment-experienced adult and pediatric patients 3 years and older with genotype 1, 2, 4, 5, or 6, without cirrhosis or with compensated cirrhosis (Child-Pugh A), who previously have not been treated with an HCV NS3/4a protease inhibitor or NS5A inhibitor***.
- Treatment-experienced adult and pediatric patients 3 years and older with genotype 3, without cirrhosis or with compensated cirrhosis (Child-Pugh A), who previously have not been treated with an HCV NS3/4a protease inhibitor or NS5A inhibitor***.

* 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.

Black Box Warning

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 who were not receiving HBV antiviral therapy, 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.

Product Availability

Oral tablet
Brand: (Mavyret) glecaprevir 100 mg and pibrentasvir 40 mg
Oral pellets in unit-dose packets
Brand: (Mavyret) glecaprevir 50 mg and pibrentasvir 20 mg

Policy/Criteria

It is the policy of Western Sky Community Care (WSCC) that **Mavyret** is **medically necessary** when the following criteria are met:

1. **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. Age ≥ 3 years*
     3. Life expectancy ≥ 12 months with HCV treatment (this can be assumed unless lower life expectancy explicitly stated in chart notes or member diagnosed with hepatocellular carcinoma);
     4. If cirrhosis is present, confirmation of Child-Pugh A status;
     5. Member is NOT treatment-experienced with both NS3/4A protease inhibitor AND NS5A inhibitors, such as combination therapies including, Viekira Pak, and Zepatier;
     6. ****Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (*see Appendix C for reference*);
     7. ****Dose as follows (a, b, or c):
        a. For pediatric patients age at least 3 years old but less than 12 years old:
           i. If weighs less than 20 kg: 150mg/60mg (three 50 mg/20mg packets of oral pellets) per day
           ii. If weighs 20 kg to less than 30 kg: 200mg/80mg (Four 50 mg/20 mg packets of oral pellets) per day
           iii. If weighs 30 kg to less than 45 kg: 250mg/100mg (Five 50 mg/20 mg packets of oral pellets) per day
           iv. If weighs 45 kg or greater: 300mg/120mg (three 100mg/40mg tabs) per day
        b. For pediatric patients age 12 years or older: 300mg/120mg (three 100mg/40mg tabs) per day
        c. For adults: 300mg/120mg (three 100mg/40mg tabs) per day
     8. Member has no contraindications to glecaprevir/pibrentasvir such as:
        a. Patients with severe hepatic impairment (Child-Pugh C)
        b. Co-administration with atazanavir or rifampin

     Approval duration: generally 8 weeks but up to a total of 16 weeks* *(see appendices C and D)* ****If treatment regimen varies in dosing or interval from FDA or AASLD-IDSA guideline recommendations but it is documented on PA request/office chart notes that requested regimen is product of consultation with Project ECHO—please approve regimen.**

   - **B. Other diagnoses/indications**

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.
2. **If denial is likely please reach out to prescriber's office for peer-to-peer.**

2. Continued Therapy

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

1. Must meet both of the following (i and ii):
    i. Documentation supports that member is currently receiving Mavyret for chronic HCV infection AND
1. Member is responding positively to therapy;
9. ****Dose as follows (a, b, or c):
    a. For pediatric patients age at least 3 years old but less than 12 years old:
        i. If weighs less than 20 kg: 150mg/60mg (three 50 mg/20mg packets of oral pellets) per day
        ii. If weighs 20 kg to less than 30 kg: 200mg/80mg (Four 50 mg/20 mg packets of oral pellets) per day
        iii. If weighs 30 kg to less than 45 kg: 250mg/100mg (Five 50 mg/20 mg packets of oral pellets) per day
        iv. If weighs 45 kg or greater: 300mg/120mg (three 100mg/40mg tabs) per day
    b. For pediatric patients age 12 years or older: 300mg/120mg (three 100mg/40mg tabs) per day
    c. For adults: 300mg/120mg (three 100mg/40mg tabs) per day

Approval duration: up to a total of 16 weeks *(Approved duration should be consistent with FDA-approved dosing and/or IDSA-AASLD guidelines; (see appendices C and D))* ****If treatment regimen varies in dosing or interval from FDA or AASLD-IDSA guideline recommendations but it is documented on PA request/office chart notes that requested regimen is product of consultation with Project ECHO—please approve regimen.**

B. Other diagnoses/indications:

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.
2. **If denial is likely please reach out to prescriber's office for peer-to-peer.**

3. 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 policies –CP.PMN.53 for Medicaid 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.

Appendices

Appendix A: Abbreviation/Acronym Key

AASLD: American Association for the Study of Liver Diseases
APRI: AST to platelet ratio
FDA: Food and Drug Administration
FIB-4: Fibrosis-4 index
HBV: hepatitis B virus
HCC: hepatocellular carcinoma
HCV: hepatitis C virus
HIV: human immunodeficiency virus
IDSA: Infectious Diseases Society of America
IQR: interquartile range
MRE: magnetic resonance elastography
NS3/4A, NS5A/B: nonstructural protein
PegIFN: pegylated interferon
RBV: ribavirin
RNA: ribonucleic acid

***Serologic tests:**

FibroTest (available through Quest as FibroTest or LabCorp as FibroSure)
FIBROSpect II (available through Prometheus Laboratory)
APRI (AST to platelet ratio index)
FIB-4 (Fibrosis-4 index: includes age, AST level, platelet count)

†Radiologic tests:

FibroScan (transient elastography)
MRE (magnetic resonance elastography)

‡Liver biopsy (histologic scoring systems):

METAVIR F3/F4 is equivalent to Knodell, Scheuer, and Batts-Ludwig F3/F4 and Ishak F4-5/F5-6
METAVIR fibrosis stages: F0 = no fibrosis; F1 = portal fibrosis without septa; F2 = few septa; F3 = numerous septa without cirrhosis; F4 = cirrhosis

Appendix B: 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***Additional PIs no longer recommended that have been discontinued*

Appendix C: Mavyret treatment duration

Genotype	Treatment Naïve Patients	Duration
1, 2, 3, 4, 5, 6	No Cirrhosis	8 wk
	Compensated Cirrhosis (Child-Pugh A)	8 wk

Genotype	Liver status	Treatment Experienced Patients	Duration
1	No Cirrhosis	An NS5A inhibitor without prior treatment with an NS3/4A protease inhibitor	16 wk
		An NS3/4A PI without prior treatment with an NS5A inhibitor	12 wk
	Compensated Cirrhosis*	An NS5A inhibitor without prior treatment with an NS3/4A protease inhibitor	16 wk
		An NS3/4A PI2 without prior treatment with an NS5A inhibitor	12 wk
1, 2, 4, 5, 6	No Cirrhosis	IFN ribavirin, and/or sofosbuvir, but no prior treatment experience with an HCV NS3/4A PI or NS5A inhibitor	8 wk
	Compensated Cirrhosis*	IFN ribavirin, and/or sofosbuvir, but no prior treatment experience with an HCV NS3/4A PI or NS5A inhibitor	12 wk
3	No Cirrhosis	IFN ribavirin, and/or sofosbuvir, but no prior treatment experience with an HCV NS3/4A PI or NS5A inhibitor	16 wk
	Compensated Cirrhosis*		

*Child-Pugh A

Appendix D: AASLD-IDSA Recommended Regimens and Treatment Durations
https://www.hcvguidelines.org/

Appendix E:
Any of the following meet the definition for cirrhosis per NM state directives:

- APRI >= 1.0
- Fib-4 >= 3.25
- Transient Elastography Score >= 12.5 dP3 (F4 equivalent)
- Fibrotest >= 0.73 (f4 equivalent) OR Fibrometer with F4 predominance
- Radiographic imaging or physical exam findings consistent with cirrhosis
- Liver biopsy confirming a METAVIR score of F4

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

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Revision Log

Reviews, Revisions, and Approvals	Date	Approval Date
New clinical policy created for WSCC based on New Mexico requirements	11/1/18	11/1/18
Added provision for approval of drug dosing and interval (despite not meeting AASLD and IDSA recommended guidelines) if regimen is recommended/requested after consultation with Project ECHO; added Project ECHO to references;	1/25/19	1/25/19
Renamed clinical policy per corporate guidelines; Changed from NM.CP.PHAR.01 to NM.CP.PPA.01; Name presented at WSCC P&T Committee;	3/20/19	3/20/19
Edited FDA approved indications; Edited age requirement to Age ≥ 12 years and added weight of at least 45 kg for pediatric members; updated references section; Approved by WSCC Pharmacy and Therapeutics Committee on 7/31/2019	7/23/19	7/31/19

Reviews, Revisions, and Approvals	Date	Approval Date
Edited Mavyret treatment duration for HCV Genotype 1-6 in patients with Compensated Cirrhosis (Child-Pugh A) from 12 weeks to 8 weeks. ; updated reference section;	1/29/20	1/29/20
Added additional direction for life expectancy > 12 months to be assumed unless explicitly stated in chart notes or member has diagnosis of hepatocellular carcinoma. Edited documentation to be submitted section to align with other Hepatitis C Drug criteria.	6/26/20	
Reviewed and approved by WSCC P&T Committee.		7/8/20
Edited criteria to match updated directive from NM HSD, MAD Supplement 20-13 to include updated forms. Updated references to reflect this change in NM Medicaid direction.	1/12/21	
Annual review. Removed requirement for genotype, as drug is pangenomic. Reviewed and approved by WSCC P&T Committee.		1/20/21
Updated age limit based on FDA approval for pediatric patients more than or equal to 3 years of age. Updated approvable dosing limits based on age and weight for pediatric patients. Edited references and links to NM HCV Uniform HCV checklist.	10/11/21	
Updated indications to include genotype 3. Reviewed and approved by WSCC P&T Committee.		10/13/21
Annual review. Reviewed and approved by WSCC P&T Committee.		1/12/22
Updated dosing portion from “Dose does not exceed” to “Dose as follows” to prevent underdosing for children.	10/10/22	
Updated wording on dosage. Reviewed and approved by WSCC P&T Committee.		10/12/22
Annual Review. Updated References. Removed requirement for Drug Authorization Form and Uniform New Mexico HCV Checklist. Reviewed and approved by WSCC P&T Committee.	1/9/23	1/11/23