

Clinical Policy: Dasabuvir, Ombitasvir, Paritaprevir, Ritonavir (Viekira XR, Viekira Pak)

Reference Number: GA.PMN.12

Effective Date: 12/16

Last Review Date: 2/19

Line of Business: Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

Viekira XR and Viekira Pak include a hepatitis C virus nonnucleoside NS5B polymerase inhibitor (dasabuvir), a hepatitis C virus NS5A inhibitor (ombitasvir), a hepatitis C virus NS3/4A protease inhibitor (paritaprevir), and a CYP3A inhibitor (ritonavir) that inhibits CYP3A mediated metabolism of paritaprevir, thereby providing increased plasma concentration of paritaprevir.

FDA Approved Indication(s)

Viekira XR and Viekira Pak are indicated for the treatment of adult patients with chronic HCV:

- Genotype 1b infection without cirrhosis or with compensated cirrhosis;
- Genotype 1a infection without cirrhosis or with compensated cirrhosis for use in combination with ribavirin.

Policy/Criteria

It is the policy of health plans affiliated with Centene Corporation® that Viekira XR/Viekira Pak 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 hepatitis C virus (HCV) infection as evidenced by detectable HCV ribonucleic acid (RNA) levels over a six-month period;
2. Age \geq 18 years;
3. Confirmed HCV genotype is 1;
*Chart note documentation and copies of labs results are required
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. Failure of Mavyret^{®/™}, unless contraindicated or clinically significant adverse effects are experienced.

7. At the time of request, member has none of the following contraindications to Mavyret (a or b):
 - a. Decompensated cirrhosis (Child-Pugh B or C) confirmed by lab findings and clinical notes;
 - b. Coadministration with efavirenz or atazanavir;
**See Appendix F for additional details on acceptable contraindications*
8. Life expectancy \geq 12 months with HCV treatment;
9. Prescribed regimen is consistent with an FDA or AASLD-IDSAs recommended regimen (*see Appendix D and E for reference*);
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 F*);
11. If HCV/human immunodeficiency virus (HIV)-1 co-infection, member is or will be on a suppressive antiretroviral drug regimen to reduce the risk of HIV-1 protease inhibitor drug resistance;
12. Dose does not exceed:
 - a. For Viekira Pak: ombitasvir/paritaprevir/ritonavir 25 mg/150 mg/100 mg (2 tablets) once daily and dasabuvir 500 mg (1 tablet) twice daily;
 - b. For Viekira XR: dasabuvir/ombitasvir/paritaprevir/ritonavir 600 mg/24.99 mg/150mg/99.99 mg (3 tablets) per day.
13. Member has none of the following contraindications:
 - a. Moderate to severe hepatic impairment (Child-Pugh B and C);
 - b. Hypersensitivity to ritonavir (e.g., toxic epidermal necrolysis [TEN] or Stevens-Johnson syndrome);
 - c. Co-administration with drugs that are highly dependent on cytochrome P450 (CYP) 3A for clearance, moderate or strong inducers of CYP3A, strong inducers of CYP2C8, and drugs that are strong inhibitors of CYP2C8 as follows: alfuzosin HCL, ranolazine, dronedarone, carbamazepine, phenytoin, phenobarbital, colchicine, gemfibrozil, rifampin, lurasidone, pimozide, ergotamine, dihydroergotamine, methylergonovine, ethinyl estradiol-containing medications such as combined oral contraceptives, cisapride, St. John's Wort, lovastatin, simvastatin, efavirenz, sildenafil when dosed as Revatio for pulmonary arterial hypertension; triazolam, orally administered midazolam;
 - d. If prescribed with ribavirin, member has none of the following contraindications:
 - i. Pregnancy or possibility of pregnancy - member or partner;
 - ii. Hypersensitivity to ribavirin;
 - iii. Coadministration with didanosine;
 - iv. Significant/unstable cardiac disease;
 - v. Hemoglobinopathy (e.g., thalassemia major, sickle cell anemia);
 - vi. Hemoglobin $<$ 8.5 g/dL.

Approval duration: up to a total of 24 weeks*

(*Approved duration should be consistent with a regimen in Appendix D or E)

B. Other diagnoses/indications: Refer to CP.PHAR.53 – No Coverage Criteria/Off-Label Use Policy if diagnosis is NOT listed in section I.

II. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AASLD: American Association for the Study of Liver Diseases	MRE: magnetic resonance elastography
APRI: AST to platelet ratio	NS3/4A, NS5A/B: nonstructural protein
CTP: Child Turcotte Pugh	Peg-IFN: pegylated interferon
CrCl: creatinine clearance	PI: protease inhibitor
FDA: Food and Drug Administration	RBV: ribavirin
FIB-4: Fibrosis-4 index	RNA: ribonucleic acid
HCC: hepatocellular carcinoma	
HCV: hepatitis C virus	
IDSA: Infectious Diseases Society of America	

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/Maximum Dose
Mavyret™ (glecaprevir/pibrentasvir)	Treatment-naïve chronic HCV infection: Genotypes 1, 2, 3, 4, 5, or 6 Without cirrhosis: Three tablets PO QD for 8 weeks With compensated cirrhosis: Three tablets PO QD for 12 weeks	Mavyret: glecaprevir 300mg/pibrentasvir 120mg (3 tablets) per day
Mavyret™ (glecaprevir/pibrentasvir)	Treatment-experienced with IFN/pegIFN+RBV+/- sofosbuvir chronic HCV infection: Genotypes 1, 2, 4, 5, or 6 Without cirrhosis: Three tablets PO QD for 8 weeks With compensated cirrhosis: Three tablets PO QD for 12 weeks	Mavyret: glecaprevir 300mg/pibrentasvir 120mg (3 tablets) per day
Mavyret™ (glecaprevir/pibrentasvir)	Treatment-experienced with IFN/pegIFN+RBV+/- sofosbuvir chronic HCV infection: Genotypes 3	Mavyret: glecaprevir 300mg/pibrentasvir 120mg (3 tablets) per day

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Drug Name	Dosing Regimen	Dose Limit/Maximum Dose
	Without cirrhosis or with compensated cirrhosis: Three tablets PO QD for 16 weeks	
Mavyret™ (glecaprevir/pibrentasvir)	Treatment-experienced with NS5A inhibitor without prior NS3/4A protease inhibitor chronic HCV infection: Genotype 1 Without cirrhosis or with compensated cirrhosis: Three tablets PO QD for 16 weeks	Mavyret: glecaprevir 300mg/pibrentasvir 120mg (3 tablets) per day
Mavyret™ (glecaprevir/pibrentasvir)	Treatment-experienced with NS3/4A protease inhibitor without prior NS5A inhibitor chronic HCV infection: Genotype 1 Without cirrhosis or with compensated cirrhosis: Three tablets PO QD for 12 weeks	Mavyret: glecaprevir 300mg/pibrentasvir 120mg (3 tablets) per day
Mavyret™ (glecaprevir/pibrentasvir)		Mavyret: glecaprevir 300mg/pibrentasvir 120mg (3 tablets) per day

Therapeutic alternatives are listed as Brand Name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications

Viekira XR and Viekira Pak are contraindicated in:

- Patients with moderate to severe hepatic impairment (Child-Pugh B and C) due to risk of potential toxicity
- If Viekira XR or Viekira is administered with RBV, the contraindications to RBV also apply to this combination regimen. Refer to the RBV prescribing information for a list of contraindications for RBV.
- Co-administration with:
 - Drugs that are highly dependent on CYP3A for clearance and for which elevated plasma concentrations are associated with serious and/or life-threatening events
 - Drugs that are moderate or strong inducers of CYP3A and strong inducers of CYP2C8 and may lead to reduced efficacy of Viekira XR and Viekira Pak
 - Drugs that are strong inhibitors of CYP2C8 and may increase dasabuvir plasma concentrations and the risk of QT prolongation

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Appendix D: Approximate Scoring Equivalencies using METAVIR F3/F4 as Reference

Fibrosis/ Cirrhosis	Serologic Tests*				Radiologic Tests†		Liver Biopsy‡	
	Fibro Test	FIBRO Spect II	APRI	FIB 4	FibroScan (kPa)	MRE (kPa)	METAVIR	Ishak
Advanced fibrosis	≥0.59	≥42	>1.5	>3.25	≥9.5	≥4.11	F3	F4-5
Cirrhosis	≥0.75	≥42	>1.5	>3.25	≥12.0	≥4.71	F4	F5-6

*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 (ultrasound-based 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 E: 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

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Appendix F: 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.
- Acceptable medical justification for inability to use Mavyret (preferred product):
 - Severe hepatic disease (Child-Pugh C): use of Mavyret is not recommended due to higher exposures of glecaprevir and pibrentasvir.
 - Moderate hepatic disease (Child-Pugh B): although not an absolute contraindication, use of Mavyret is not recommended in patient with moderate hepatic disease (Child-Pugh B) due to lack of safety and efficacy data.
 - Following administration of Mavyret in HCV infected subjects with *compensated* cirrhosis (Child-Pugh A), exposure of glecaprevir was approximately 2-fold and pibrentasvir exposure was similar to non-cirrhotic *HCV infected* subjects
 - At the clinical dose, compared to *non-HCV infected* subjects with *normal hepatic function*, glecaprevir AUC was 100% higher in Child-Pugh B subjects, and increased to 11-fold in Child-Pugh C subjects. Pibrentasvir AUC was 26% higher in Child-Pugh B subjects, and 114% higher in Child-Pugh C subjects
 - Drug-drug interactions with one or more of the following agents:
 - Atazanavir
 - Efavirenz
- Unacceptable medical justification for inability to use Mavyret (preferred product):
 - Black Box warning (BBW): currently or previously infected with hepatitis B virus. This BBW is not unique to Mavyret, and it applies across the entire therapeutic class of direct-acting antivirals for treatment of HCV infection. Therefore it is not a valid clinical reason not to use Mavyret.
 - Concurrent anticoagulant therapy: Fluctuations in International Normalized Ratio (INR) have been observed in warfarin recipients who were also receiving treatment for HCV infections. This BBW is not unique to Mavyret, and it applies across the entire therapeutic class of direct-acting antivirals for treatment of HCV infection..
 - Drug-drug interactions with one or more of the following agents:
 - Rifampin, carbamazepine, or St. John's wort:
 - These drug-drug interactions are not unique to Mavyret, and they apply across the entire therapeutic class of direct-acting antivirals for the treatment of HCV infection.

III. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose	Reference
Genotype 1a: Treatment-naïve or treatment-experienced with pegIFN/RBV without cirrhosis	Viekira Pak/XR plus weight-based RBV for 12 weeks	Viekira Pak: paritaprevir 150 mg /ritonavir 100mg/ ombitasvir 25 mg per day; dasabuvir 500 mg per day Viekira XR: paritaprevir 150 mg /ritonavir 100 mg/ ombitasvir 25 mg/dasabuvir 600 mg per day	1) FDA-approved labeling 1) 2) AASLD-IDSA (updated September 2017)
Genotype 1b: Treatment-naïve or treatment-experienced with pegIFN/RBV with or without compensated cirrhosis	Viekira Pak/XR for 12 weeks		1) FDA-approved labeling 2) 2) AASLD-IDSA (updated September 2017)

*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.
The AASLD/IDSA HCV guidance updated September 2017 no longer recommends use of Viekira Pak/XR for the treatment of genotype 1a with compensated cirrhosis.*

IV. Product Availability

Drug	Availability
Paritaprevir/ ritonavir/ ombitasvir/ dasabuvir (Viekira Pak)	Tablets: paritaprevir 75 mg, ritonavir 50 mg, ombitasvir 12.5 mg Tablets: dasabuvir 250 mg <i>*Viekira Pak is dispensed in a monthly carton for a total of 28 days of therapy. Each monthly carton contains four weekly cartons. Each weekly carton contains seven daily dose packs.</i>
Paritaprevir/ ritonavir/ ombitasvir/ dasabuvir (Viekira XR)	Extended-release tablets: dasabuvir 200 mg, ombitasvir 8.33 mg, paritaprevir 50 mg, ritonavir 33.33 mg <i>*Viekira XR is dispensed in a monthly carton for a total of 28 days of therapy. Each monthly carton contains four weekly cartons. Each weekly carton contains seven daily dose packs.</i>

V. References

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Reviews, Revisions, and Approvals	Date	Approval Date
<p>New policy created, split from CP.PHAR.17 Hepatitis C Therapies. HCV RNA levels over six-month period added to confirm infection is chronic. Life expectancy “≥12 months if HCC and awaiting transplant” is modified to indicate “≥12 months with HCV therapy.” Testing criteria reorganized by “no cirrhosis”/“cirrhosis;” HCC population is included under “cirrhosis” and broadened to incorporate HCC amenable to curative measures (resection, ablation, transplant). Methods to diagnose fibrosis/cirrhosis are modified to require presence of HCC, liver biopsy or a combination of one serologic and one radiologic test. Serologic and radiologic tests are updated and correlated with METAVIR per Appendix B. Removed creatinine clearance restriction. Dosing regimens are presented in Appendix D and E per AASLD guidelines and FDA-approved indications. The initial approval period is shortened to 8 weeks.</p>	08/16	09/16
<p>Removed criteria regarding medication prescribed by a specialist Remove criteria regarding having HCC or advanced liver disease Removed criteria regarding medication adherence program Removed criteria regarding sobriety from alcohol/illicit drugs</p>	10/16	10/16
<p>Added availability of full course of therapy as initial therapy consistent with appendix recommendation for initial criteria Removed continuation criteria</p>	4/17	
<p>Added preferencing information requiring Mavyret for FDA-approved indications. Exception made to require Hep B screening for all patients prior to treatment. Added do not exceed dosing restrictions</p>	9/17	
<p>Annual review. No changes made.</p>	3/18	
<p>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. Added new preferred treatment tables that includes dosage and frequency based on genotype for Mavyret. Removed background sections. Updated general information and contraindication section to be consistent with corporate HCV policies.</p>	2/21/19	

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

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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.

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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.

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