Clinical Policy: Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir (Viekira Pak)

Reference Number: IL.PHAR.278
Effective Date: 09.16
Last Review Date: 9.14.21
Line of Business: Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Dasabuvir/paritaprevir/ritonavir/ombitasvir (Viekira Pak®) is a combination of ombitasvir, a hepatitis C virus (HCV) NS5A inhibitor, paritaprevir, a hepatitis C virus NS3/4A protease inhibitor, ritonavir, a CYP3A inhibitor and dasabuvir, a hepatitis C virus non-nucleoside NS5B palm polymerase inhibitor.

FDA Approved Indication(s)

Viekira Pak is indicated for the treatment of adult patients with chronic HCV:

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

Policy/Criteria

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

It is the policy of health plans affiliated with Centene Corporation® that Viekira XR or Viekira Pak 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 serum HCV RNA levels by quantitative assay in the last 6 months;
2. Confirmed HCV genotype is 1;
   **Chart note documentation and copies of lab results are required*
3. The prescriber can be any practitioner licensed to prescribe, or licensed to prescribe in collaboration with a physician who holds a current unrestricted license to practice medicine. If the prescriber is NOT a gastroenterologist, hepatologist, transplant hepatologist, or infectious disease specialist, the prescriber must engage in a one-time consultation with one of these specialists within the 3 months prior to the request for prior authorization. This one-time consultation may be via telephone, video-conference, or telehealth technology. The records containing a specialist recommendation for treatment with a DAA regimen must be submitted with the request for prior approval.
4. Age ≥ 12 years;

5. Patient's Metavir/fibrosis score must be documented in the request for prior approval. The patient's Metavir/fibrosis score can be determined based on Liver Biopsy, Transient Elastography (FibroScan ®), FibroTest®/FibroSure®, or FibroMeter™.
6. Lab test reports, completed within 3 months prior to the request for prior approval, unless otherwise noted:
   a. Baseline quantitative HCV RNA level (within 1 year of request for prior approval)
   b. ALT and AST
   c. CBC
   d. GFR
   e. INR, albumin, and bilirubin, for stage 4 fibrosis only
   f. Negative HBV screen; or, if positive, quantitative HBV DNA and verification of treatment regimen
7. If cirrhosis is present, confirmation of Child-Pugh A status;
8. Member must use sofosvubir/velpatasvir (Epclusa®) (*authorized generic preferred*) or Mavyret®, unless clinically significant adverse effects are experienced or both are contraindicated (*see Appendix F*);
   *Coadministration with omeprazole up to 20 mg is not considered acceptable medical justification for inability to use Epclusa
9. Life expectancy ≥ 12 months with HCV treatment; Patient is able to make appropriate decisions about treatment and comply with dosing and other instructions, and is capable of completing therapy as prescribed. The prescriber must provide a copy of a signed patient commitment letter for all hepatitis C treatment regimens
10. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (*see Section V Dosage and Administration for reference)*;
11. If HCV/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 ombitasvir/paritaprevir/ritonavir 12.5 mg/75 mg/50 mg (2 tablets) once daily and dasabuvir 250 mg (1 tablet) twice daily.

Approval duration: up to a total of 12 weeks*

*(*Approved duration should be consistent with a regimen in Section V Dosage and Administration)*

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.

II. Continued Therapy

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Must meet both of the following (i and ii):

i. Documentation supports that member is currently receiving Viekira Pak for chronic HCV infection and has recently completed at least 60 days of treatment with Viekira Pak;
ii. Confirmed HCV genotype is 1;

2. Member is responding positively to therapy;
3. Dose does not exceed ombitasvir/paritaprevir/ritonavir 12.5 mg/75 mg/50 mg (2 tablets) once daily and dasabuvir 250mg (1 tablet) twice daily.

Approval duration: up to a total of 12 weeks*

*(*Approved duration should be consistent with a regimen in Section V Dosage and Administration)*

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.

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 policies – CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

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

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
sofosbuvir/ velpatasvir (Epclusa®)	Treatment-naïve or treatment-experienced with pegIFN/RBV without cirrhosis or with compensated cirrhosis: **Genotype 1** One tablet PO QD for 12 weeks	Epclusa: sofosbuvir 400 mg/ velpatasvir 100 mg (1 tablet) per day
Mavyret®	Treatment-naïve: **Genotype 1**	Mavyret: glecaprevir 300 mg/pibrentasvir

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
(glecaprevir/ pibrentasvir)	Without cirrhosis or with compensated cirrhosis: Three tablets PO QD for 8 weeks	120 mg (3 tablets) per day
Mavyret® (glecaprevir/ pibrentasvir)	Treatment-experienced with IFN/pegIFN + RBV +/- sofosbuvir: **Genotype 1** Without cirrhosis: Three tablets PO QD for 8 weeks With compensated cirrhosis: Three tablets PO QD for 12 weeks	Mavyret: glecaprevir 300 mg/pibrentasvir 120 mg (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/Boxed Warnings

- Contraindication(s): Viekira Pak is contraindicated in:
  - Patients with moderate to severe hepatic impairment (Child-Pugh B and C) due to risk of potential toxicity
  - If 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
    - Moderate or strong inducers of CYP3A and strong inducers of CYP2C8 and may lead to reduced efficacy of Viekira Pak
    - Strong inhibitors of CYP2C8 and may increase dasabuvir plasma concentrations and the risk of QT prolongation
  - Patients with known hypersensitivity to ritonavir (e.g., toxic epidermal necrolysis (TEN) or Stevens-Johnson syndrome).
- Boxed warning(s): risk of hepatitis B virus reactivation in patients coinfected with HCV and HBV

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
Epclusa*	Velpatasvir	Sofosbuvir			

Brand Name	Drug Class				
	NS5A Inhibitor	Nucleotide Analog NS5B Polymerase Inhibitor	Non-Nucleoside NS5B Palm Polymerase Inhibitor	NS3/4A Protease Inhibitor (PI)	CYP3A Inhibitor
Harvoni*	Ledipasvir	Sofosbuvir			
Mavyret*	Pibrentasvir			Glecaprevir	
Sovaldi		Sofosbuvir			
Viekira PAK*	Ombitasvir		Dasabuvir	Paritaprevir	Ritonavir
Vosevi*	Velpatasvir	Sofosbuvir		Voxilaprevir	
Zepatier*	Elbasvir			Grazoprevir	

*Combination drugs

Appendix F: General Information

- Acceptable medical justification for inability to use Mavyret (preferred product):
  - Drug-drug interactions with atazanavir
- Acceptable medical justification for inability to use Epclusa (preferred product):
  - In patients indicated for co-administration of Epclusa with ribavirin: contraindications to ribavirin
  - In patients indicated for co-administration with amiodarone: serious symptomatic bradycardia in patients taking amiodarone, with cardiac monitoring recommended.
- Unacceptable medical justification for inability to use Epclusa (preferred product): o Coadministration with omeprazole up to 20 mg is not considered acceptable medical justification for inability to use Epclusa.
  - Per the Epclusa Prescribing Information: "If it is considered medically necessary to coadminister, Epclusa should be administered with food and taken 4 hours before omeprazole 20 mg.
- 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.
- For patients with HCV/HIV-1 (human immunodeficiency virus type-1) co-infection, the patient should be on a suppressive antiretroviral drug regimen to reduce the risk of HIV-1 protease inhibitor drug resistance.
- 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

	1 Point	2 Points	3 Points
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.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose	Reference
Genotype 1a: Treatment-naive or treatment-experienced with pegIFN/RBV without cirrhosis	Viekira Pak plus weight-based RBV for 12 weeks	Viekira Pak: paritaprevir 150 mg /ritonavir 100mg/ om bitasvir 25 mg per day; dasabuvir 500 mg per day	FDA-approved labeling
Genotype 1b: Treatment-naïve or treatment-experienced with pegIFN/RBV with or without compensated cirrhosis	Viekira Pak for 12 weeks		FDA-approved labeling

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 for the treatment of genotype 1a with compensated cirrhosis***Product Availability**

- Tablets: paritaprevir 75 mg, ritonavir 50 mg, ombitasvir 12.5 mg
- Tablets: dasabuvir 250 mg

**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.*

VI. References

1. Viekira Pak Prescribing Information. North Chicago, IL: Abbvie Pharmaceuticals Corp; December 2019. Available at https://www.rxabbvie.com/. Accessed April 15, 2021.
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 March 12, 2021. Available at: https://www.hcvguidelines.org/. Accessed April 15, 2021.
3. CDC. Heaptitis C Q&As for health professionals. Last updated August 7, 2020. Available at: https://www.cdc.gov/hepatitis/hcv/hcvfaq.htm. Accessed April 15, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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.	08.16	09.16
Policy converted to new template. Added requirement for prevention of HBV reactivation. Consolidated appendix D and E into dosing and administration in section V; Extended initial approval duration to full regimen; deleted adherence requirement in continued therapy section; added maximum dose requirement, added documentation of positive response to therapy and continuity of care, and removed CIs in section II, added reference column in section V. Added preferencing information requiring Mavyret for FDA-approved indications. Safety criteria was 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.	08.17	09.17
3Q 2018 annual review: removed requirement for HBV verification; removed requirement to check for ART for HCV/HIV co-infection; expanded duration of tx required for COC from 30 days 60 days; required verification of genotype for COC; removed conditional requirement for RBV CI; reduced maximum approval duration from 24 weeks to 12 weeks per AASLD/IDSA September 2017 guidance; references reviewed and updated.	05.22.18	08.18
Removed requirement for advanced fibrosis or other candidacy for therapy following approved clinical guidance and removed sobriety requirement.	2.26.19	4.19
2Q2021 annual review: **Removed** removed discontinued Viekira XR from policy; **Added** new prescriber requirement to include a "provider who has expertise in treating HCV based on a certified training program; **Added** Appendix G (Healthcare Provider HCV Training); **removed** documented sobriety from alcohol and illicit IV drugs for ≥ 6 months prior to starting therapy; **Added** Member must use sofosvubir/velpatasvir (Epclusa®) (*authorized generic preferred*) or Mavyret®, unless clinically significant adverse effects are	6.17.21	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
experienced or both are contraindicated; **Added** If HCV/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; **Updated** section Dosing and Administration; ; **removed** medical justification for ability to use Mavyret from Appendix F; **removed** documented sobriety from alcohol and illicit IV drugs for ≥ 6 months prior to starting therapy; **Removed** *Appendix D: Approximate Scoring Equivalencies using METAVIR F3/F4;* ; references reviewed and updated; reviewed and updated references		
Included reference to Appendix F with addition of contraindications that would warrant bypassing preferred agents; references reviewed and updated.	9.14.21	
4Q 2022 annual review: updated section I to reflect HFS criteria; added omeprazole coadministration as unacceptable rationale for not using preferred Epclusa to criteria and Appendix F; references reviewed and updated	11.17.22	

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.

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.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.