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

Reference Number: CP.PHAR.278
Effective Date: 09/16
Last Review Date: 09/17
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 XR, Viekira Pak™) is a combination of ombitasvir, a hepatitis C virus 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

Viekira Pak is indicated for the treatment of adult patients with chronic hepatitis C virus (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 (including office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of health plans affiliated with Centene Corporation® that Viekira Pak and Viekira XR are **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 multiple detectable HCV RNA (ribonucleic acid) levels in the last 6 months;
2. Confirmed HCV genotype is 1;
3. Prescribed by or in consultation with a gastroenterologist, hepatologist, or infectious disease specialist;
4. Age ≥ 18 years;
5. Member has no cirrhosis or compensated cirrhosis;
6. Life expectancy ≥ 12 months with HCV treatment;
7. Documented sobriety from alcohol and illicit IV drugs for ≥ 6 months prior to starting therapy, if applicable;
8. Advanced liver disease defined as a or b:
   a. Advanced fibrosis indicated by i or ii:
      i. Liver biopsy showing a METAVIR score of F3 or equivalent (Knodell, Scheuer, Batts-Ludwig – F3; Ishak – F4/5);
      ii. One serologic test and one radiologic test showing an equivalent score to METAVIR F3 per Appendix C;

b. Cirrhosis indicated by i, ii or iii:
   i. Hepatocellular carcinoma (HCC) - and the HCC is amenable to resection, ablation or transplant;
   ii. Liver biopsy showing a METAVIR score of F4 or equivalent (Knodell, Scheuer, Batts-Ludwig – F4; Ishak - F5/6);
   iii. Both of the following:
      a) One serologic test showing an equivalent score to METAVIR F4 per Appendix C;
      b) One radiologic test showing an equivalent score to METAVIR F4 per Appendix C or other radiologic test showing evidence of cirrhosis (e.g., portal hypertension);

9. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (*see Section V Dosage and Administration for reference)*;
10. If member is without cirrhosis or with compensated cirrhosis (Child-Pugh A): contraindication or intolerance to Mavyret;
11. Member agrees to participate in a medication adherence program meeting both of the following components;
    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;
12. 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;
13. 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 B*);
14. At the time of request, member has none of the following contraindications:
    a. If prescribed with ribavirin, at the time of request, member has none of the following contraindications:
       i. Pregnancy;
       ii. For Rebetol: creatinine clearance < 50 mL/min;
15. Dose does not exceed:
    a. For Viekira Pak: ombitasvir/paritaprevir/ritonavir 12.5 mg/75 mg/50 mg (2 tablets) once daily and dasabuvir 250 mg (1 tablet) twice daily;
    b. For Viekira XR: dasabuvir/ombitasvir/paritaprevir/ritonavir 200 mg/8.33 mg/50mg/33.33 mg (3 tablets) per day.

Approval duration: up to 24 weeks*
*(*Approved duration should be consistent with a regimen in Section V Dosage and Administration)*

B. Other diagnoses/indications

1. Refer to 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 Centene benefit, or documentation supports that member is currently receiving Viekira XR or Viekira Pak for chronic hepatitis C virus infection and has received this medication for at least 30 days;
2. 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;
3. Member is responding positively to therapy (e.g. decreased HCV RNA level, no unacceptable toxicity);
4. Dose does not exceed:
   a. For Viekira Pak: ombitasvir/paritaprevir/ritonavir 12.5 mg/75 mg/50 mg (2 tablets) once daily and dasabuvir 250mg (1 tablet) twice daily;
   b. For Viekira XR: dasabuvir/ombitasvir/paritaprevir/ritonavir 200 mg/8.33 mg/50 mg/33.33 mg (3 tablets) per day.

Approval duration: up to a total of 24 weeks*

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

B. Other diagnoses/indications

1. Refer to 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 – CP.PHAR.57 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALT: alanine aminotransferase
APRI: AST to platelet ratio
AASLD: American Association for the Study of Liver Diseases
CYP: cytochrome P450
FDA: Food and Drug Administration
FIB-4: Fibrosis-4 index
HBeAg: hepatitis B virus envelope antigen
HBV: hepatitis B virus
HCC: hepatocellular carcinoma
HCV: hepatitis C virus
HIV: human immunodeficiency virus
IDSA: Infectious Diseases Society of America
MRE: magnetic resonance elastography
NS3/4A, NS5A/B: nonstructural protein
Peg-IFN: pegylated interferon
RBV: ribavirin

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;

- 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.

- The 2016 AASLD/IDSA treatment guideline for HBV consider ALT levels <30 U/L for men and <19 U/L for women as upper limits of normal.
- The 2016 AASLD/IDSA treatment guideline for HBV recommend adults with compensated cirrhosis, even with low levels of viremia (<2,000 IU/mL) be treated with antiviral therapy to reduce the risk of decompensation, regardless of ALT level. The recommendation extends to adults with decompensated cirrhosis be treated with antiviral therapy indefinitely regardless of HBV DNA level, HBeAg status, or ALT level to decrease the risk of worsening liver-related complications.

Appendix C: 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 (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 D: 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

Indication	Dosing Regimen	Maximum Dose	Reference
Genotype 1a: Treatment-naive or treatment-experienced with peg-IFN/RBV without cirrhosis	Viekira Pak/XR plus weight-based RBV For 12 weeks	Viekira Pak: paritaprevir 150mg /ritonavir 100mg/ ombitasvir 25mg per day; dasabuvir 500mg per day Viekira XR: paritaprevir 150mg /ritonavir 100mg/ ombitasvir 25mg/dasabuvir 600mg per day	1) FDA-approved labeling 2) AASLD-IDSA (updated April, 2017)
Genotype 1a: Treatment-naive or treatment-experienced with peg-IFN/RBV with compensated cirrhosis	Viekira Pak/XR plus weight-based RBV For 24 weeks		1) FDA-approved labeling 2) AASLD-IDSA (updated April, 2017)
Genotype 1b: Treatment-naïve or treatment-experienced with peg-IFN/RBV with or without compensated cirrhosis	Viekira Pak/XR For 12 weeks		1) FDA-approved labeling 2) AASLD-IDSA (updated April, 2017)
Genotype 1: Post-liver transplant with normal liver function and early-stage fibrosis (Metavir Stage F0-F2)	Viekira Pak/XR plus weight-based RBV For 24 weeks		AASLD-IDSA (updated April, 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.*

VI. Product Availability

Drug	Availability
Paritaprevir/ritonavir/ombitasvir + dasabuvir (Viekira Pak)	Tablets: paritaprevir 75 mg, ritonavir 50 mg, ombitasvir 12.5 mg tablets plus dasabuvir 250 mg tablets *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.
Paritaprevir/ritonavir/ombitasvir/ dasabuvir (Viekira XR)	Extended-release tablets: dasabuvir 200 mg, ombitasvir 8.33 mg, paritaprevir 50 mg, and ritonavir 33.33 mg

VII. References

1. Viekira Pak [Prescribing Information]. North Chicago, IL: Abbvie Pharmaceuticals Corp; March 2017. Available at www.viekira.com. Accessed May 11, 2017.
2. Feld JJ, Kowdkey KV, Coakley E et al. Treatment of HCV with ABT-450r-ombitasvir and dasabuvir with ribavirin. *NEJM* Apr 24,2014;370;17:1594-1603.
3. Zeuzem S, Jacobson IM, Baykal T et al. Retreatment of HCV with ABT-450r-ombitasvir and dasabuvir with ribavirin. *NEJM* Apr 24, 2014;370;17:1604-1614.
4. Poordad F, Hezode C, Trinh R, et al. ABT-450r-Ombitasvir and dasbuvir with ribavirin for hepatitis C with cirrhosis. *NEJM* May 22, 2014;370;21: 1973-1982
5. Ferenci P, Bernstein D, Lalezari J et al. ABT-450r-ombitasvir and dasabuvir with or without ribavirin for HCV. *NEJM* May 22, 2014;370;21: 1983-1992
6. Hepatitis C virus (HCV) guidance: Recommendations for testing, managing, and treating hepatitis C. AASLD-IDSA. Available at http://www.hcvguidelines.org. Accessed May 11, 2017.
7. World Health Organization (WHO) guidelines for treatment of hepatitis C. April 2014 Available at: http://apps.who.int/iris/bitstream/10665/111747/1/9789241548755_eng.pdf?ua=1&ua=1. Accessed May 11, 2017.
8. Terrault NA, Bzowej NH, Chang KM, et al. AASLD Guidelines for Treatment of Chronic Hepatitis B. Hepatology 2016; 62(1): 261-283.

Reviews, Revisions, and Approvals	Date	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).	08/16	09/16

Reviews, Revisions, and Approvals	Date	Approval Date
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.		
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

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.