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

Reference Number: GA.PMN.12
Product: Medicaid
Effective Date: 12/16
Last Review Date: 3/18 Revision Log

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

Description
The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for dasabuvir/ombitasvir/paritaprevir/ritonavir (Viekira XR™) and ombitasvir, paritaprevir, and ritonavir tablets copackaged with dasabuvir tablets (Viekira Pak®).

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. Age ≥ 18 years;
2. Diagnosis of chronic hepatitis C virus (HCV) infection as evidenced by detectable HCV ribonucleic acid (RNA) levels over a six-month period;
3. Confirmed HCV genotype is 1;
4. Life expectancy ≥ 12 months with HCV treatment;
5. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (*see Appendix D and E for reference)*;
6. Member has no cirrhosis or compensated cirrhosis;
7. If member is without cirrhosis or with compensated cirrhosis (Child-Pugh A): Mavyret is preferred unless contraindication or intolerance
8. 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*);
9. 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;
10. 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.
11. 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 gation 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.57 - Global Biopharm Policy.

Background
Description/Mechanism of Action:
Viekira XR and Viekira Pak include a hepatitis C virus nonnucleoside NS5B palm 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.

Viekira XR is a fixed dose combination, extended-release oral tablet formulation including dasabuvir, ombitasvir, paritaprevir, and ritonavir as a single tablet.

Viekira Pak is a fixed dose combination oral tablet formulation including ombitasvir, paritaprevir and ritonavir as a single tablet copackaged with dasabuvir as a tablet.

Viekira XR Formulations
Combination Bilayer Tablet, Oral (Extended Relase [ER]/Immediate Release [IR]:
ER Layer: Dasabuvir 200 mg
IR Layer: Ombitasvir 8.33 mg, paritaprevir 50 mg, ritonaivr 33.33 mg
Viekira Pak Formulations[2]

Combination Package:
IR Tablet, Oral: Ombitasvir 12.5 mg, paritaprevir 75 mg, and ritonavir 50 mg
IR Tablet, Oral: Dasabuvir 250 mg

Ribavirin Formulations[1,13]
Capsule, Oral:
Rebetol: 200 mg
Ribasphere: 200 mg
Generic: 200 mg
Solution, Oral:
Rebetol: 40 mg/mL (100 mL)
Tablet, Oral:
Copegus: 200 mg
Moderiba (includes dose packs): 200 mg, 400 mg, 600 mg
Ribasphere: 200 mg, 400 mg, 600 mg
Ribasphere RibaPak (dose packs): 200 mg, 400 mg, 600 mg
Generic: 200 mg

FDA Approved Indications:
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.

Appendices
Appendix A: Abbreviation Key
APRI: AST to platelet ratio
AASLD: American Association for the Study of Liver Diseases
CTP: Child Turcotte Pugh
CrCl: creatinine clearance
CYP: cytochrome P450
FIB-4: Fibrosis-4 index
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
RNA: ribonucleic acid

Appendix B: Approximate Scoring Equivalencies using METAVIR F3/F4 as Reference[2-10]

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 C: 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
**Additional PIs no longer recommended: Victrelis (boceprevir), Incivek (telaprevir)

Appendix D: FDA-Approved Regimens and Treatment Durations

Treatment Naive/Experienced	Genotype	Failed Treatment Regimen	Recommended Regimen *See footnotes for duration*
No Cirrhosis			
Not specified	1*	Not specified	Viekira XR/PAK + RBV† *If post-liver transplantation and METAVIR ≤F2 (this specific regimen is not covered because Centene requires METAVIR score of F3 or F4)*
	1*, 1a	Not specified	Viekira XR/PAK + RBV§
	1b	Not specified	Viekira XR/PAK§
Compensated Cirrhosis (CTP/Child-Pugh Class A)			
Not specified	1*, 1a	Not specified	Viekira XR/PAK + RBV†
	1b	Not specified	Viekira XR/PAK§

*Subtype a or b, or unknown subtype
§Treatment duration - 12 weeks
♦Treatment duration – 12 to 24 weeks

Appendix E: AASLD-IDSA Recommended Regimens and Treatment Durations

Treatment Naive/Experienced	Genotype	Failed Treatment Regimen	Recommended Regimen *See footnotes for duration*
No Cirrhosis			
Treatment naive	1a	None	Viekira XR/PAK + RBV§
	1b	None	Viekira XR/PAK§
Treatment experienced	1a, 1b	Peg-IFN/RBV	Viekira XR/PAK + RBV§
Not specified	1*	Not specified	Viekira XR/PAK + RBV† *If post-liver transplantation and METAVIR ≤F2. (Regimen is not covered because Centene requires METAVIR score of F3 or F4)*
Compensated Cirrhosis (CTP/Child-Pugh Class A)			
Treatment naive	1a	None	Viekira XR/PAK + RBV†
	1b	None	Viekira XR/PAK§
Treatment experienced	1a	Peg-IFN/RBV	Viekira XR/PAK + RBV†
	1b	Peg-IFN/RBV	Viekira XR/PAK + RBV§

*Subtype a or b, or unknown subtype
§Treatment duration - 12 weeks
†Treatment duration – 24 weeks

Appendix F: 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.

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). 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
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	10/16	10/16
Added availability of full course of therapy as initial therapy consistent with appendix recommendation for initial criteria Removed continuation criteria	4/17	
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	9/17	
Annual review. No changes made.	3/18	

References

1. Viekira XR Prescribing Information. North Chicago, IL: AbbVie, Inc.; June 2016. Available at http://www.rxabbvie.com/pdf/viekiraxr_pi.pdf. Accessed August 1, 2016.
2. Viekira Pak Prescribing Information. North Chicago, IL: AbbVie, Inc.; June 2016. Available at http://www.rxabbvie.com/pdf/viekirapak_pi.pdf. Accessed August 1, 2016.
3. AASLD-IDSA. Recommendations for testing, managing, and treating hepatitis C. http://www.hcvguidelines.org. Accessed July 12, 2016.
4. Curry MP, Nezam AH. Noninvasive assessment of hepatic fibrosis: Overview of serologic and radiographic tests. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2016. Available at UpToDate.com. Accessed July 15, 2016.
5. Fiel MI. Histologic scoring system for chronic liver disease. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2016. Available at UpToDate.com. Accessed July 15, 2016.
6. Bonder A, Afdhal N. Utilization of FibroScan in clinical practice. *Curr Gastroenterol Rep.* 2014; 16(372): 1-7. DOI 10.1007/s11894-014-0372-6.
7. Halfon P, Bourliere M, Deydier R, et al. Independent prospective multicenter validation of biochemical markers (Fibrotest–Actitest) for the prediction of liver fibrosis and activity in

patients with chronic hepatitis C: The Fibropaca study. Am J Gastroenterol. 2006; 101: 547-555. DOI: 10.1111/j.1572-0241.2006.0411.x
8. Hepatitis C Virus (HCV) FibroSure. Laboratory Corporation of America Holdings and Lexi-Comp, Inc. Available at https://www.labcorp.com. 2016. Accessed July 15, 2016.
9. Hepatitis C Virus (HCV) FibroTest-ActiTest Panel. Nichols Institute/Quest Diagnostics. Available at http://education.questdiagnostics.com/physician_landing_page. 2016. Accessed July 15, 2016.
10. Hepatitis C Virus (HCV) FIBROSpect II. Prometheus Therapeutics and Diagnostics. Available at http://www.prometheuslabs.com/Resources/Fibrospect/Fibrospect_II_Product_Detail_Sheet_FIB16005_04-16.pdf. April 2016. Accessed July 15, 2016.
11. Hsieh YY, Tung SY, Lee K, et al. Routine blood tests to predict liver fibrosis in chronic hepatitis C. World J Gastroenterol. February 28, 2012; 18(8): 746-53. doi: 10.3748/wjg.v18.i8.746.
12. Bruix J and Sherman M. Management of hepatocellular carcinoma: An update. AASLD Practice Guideline. *Hepatology*. 2011; 53(3): 1020-22.
13. Ribavirin (systemic): Drug information. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2016. Available at UpToDate.com. Accessed July 11, 2016.

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.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.