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

Reference Number: CP.CPA.288
Effective Date: 11.01.16
Last Review Date: 08.19
Line of Business: Commercial

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 (HCV) NS5A inhibitor, paritaprevir, an HCV NS3/4A protease inhibitor, ritonavir, a CYP3A inhibitor and dasabuvir, an HCV non-nucleoside NS5B palm polymerase inhibitor.

FDA Approved Indication(s)

Viekira XR/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 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 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. Prescribed by or in consultation with a gastroenterologist, hepatologist or infectious disease physician;
4. Age ≥ 18 years;
5. If cirrhosis is present, confirmation of Child-Pugh A status;
6. Member must use Harvoni® (*authorized generic or brand for 8 weeks only*), sofosvubir/velpatasvir (Epclusa®) (*authorized generic preferred*), Mavyret™, or Zepatier®, unless all are contraindicated or clinically significant adverse effects are experienced;
7. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (*see Section V Dosage and Administration for reference)*;
8. 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: 12 weeks*

*(*Approved duration should be consistent with a regimen in Section V Dosage and Administration; 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 for 24 weeks)*

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.CPA.09 for commercial.

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 XR or Viekira Pak for chronic HCV infection and has recently completed at least three quarters of the full regimen with Viekira XR or Viekira Pak;
      ii. Confirmed HCV genotype is 1;
2. Member is responding positively to therapy;
3. 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 12 weeks*

*(*Approved duration should be consistent with a regimen in Section V Dosage and Administration; 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 for 24 weeks)*

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.CPA.09 for commercial.

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.CPA.09 for commercial or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AASLD: American Association for the Study of Liver Diseases
FDA: Food and Drug Administration
HBV: hepatitis B virus
HCV: hepatitis C virus
HIV: human immunodeficiency virus
IDSA: Infectious Diseases Society of America
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
Harvoni® (sofosbuvir/ ledipasvir)	Without cirrhosis, treatment-naïve, whose HCV viral load is less than 6 million IU/mL: **Genotypes 1** One tablet PO QD for 8	Harvoni: sofosbuvir 400 mg/ ledipasvir 90 mg (1 tablet) per day
Epclusa® (sofosbuvir/ velpatasvir)	Treatment-naïve or treatment-experienced with pegIFN/RBV with or without compensated cirrhosis: **Genotype 1** One tablet PO QD for 12 weeks	Epclusa: sofosbuvir 400 mg/ velpatasvir 100 mg (1 tablet) per day
Mavyret™ (glecaprevir/ pibrentasvir)	Treatment-naïve or treatment-experienced with pegIFN/RBV: **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
Zepatier® (grazoprevir/ elbasvir)	**Genotype 1a:** Treatment-naïve or pegIFN/RBV-experienced with or without compensated cirrhosis without baseline NS5A polymorphisms at amino acid positions 28, 30, 31, or 93 One tablet PO QD for 12 weeks	One tablet (grazoprevir 100 mg/ elbasvir 50 mg) per day
Zepatier® (grazoprevir/ elbasvir)	**Genotype 1a:** Treatment-naïve or PegIFN/RBV experienced with or without compensated cirrhosis with baseline NS5A polymorphisms at amino acid positions 28, 30, 31, or 93	One tablet (grazoprevir 100 mg/ elbasvir 50 mg) per day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	One tablet PO QD plus weight-based RBV for 16 weeks	
Zepatier® (grazoprevir/ elbasvir)	**Genotype 1b:** Treatment-naïve or PegIFN/RBV experienced with or without compensated cirrhosis One tablet PO QD for 12 weeks	One tablet (grazoprevir 100 mg/ elbasvir 50 mg) per day
Zepatier® (grazoprevir/ elbasvir)	**Genotype 1a or 1b:** pegIFN/RBV/NS3 PI*‡ -experienced with or without compensated cirrhosis without baseline NS5A polymorphisms at amino acid positions 28, 30, 31, or 93 One tablet PO QD plus weight-based RBV for 12 weeks	One tablet (grazoprevir 100 mg/ elbasvir 50 mg) per day
Zepatier® (grazoprevir/ elbasvir)	**Genotype 1a or 1b:** pegIFN/RBV/NS3 PI*‡ -experienced with or without compensated cirrhosis with baseline NS5A polymorphisms at amino acid positions 28, 30, 31, or 93 One tablet PO QD plus weight-based RBV for 16 weeks	One tablet (grazoprevir 100 mg/ elbasvir 50 mg) 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 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
- Boxed warning(s): risk of hepatitis B virus reactivation in patients coinfected with HCV and HBV

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			
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

Appendix E: General Information

- 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
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/XR 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 Viekira XR: paritaprevir 150 mg /ritonavir 100 mg/ ombitasvir 25 mg/dasabuvir 600 mg per day	1) FDA-approved labeling 2) AASLD-IDSA (updated May 2018)
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) AASLD-IDSA (updated May 2018)

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.

VI. 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 **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, ritonavir 33.33 mg **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.*

VII. References

1. Viekira Pak Prescribing Information. North Chicago, IL: Abbvie Pharmaceuticals Corp; July 2018. Available at https://www.rxabbvie.com/. Accessed April 30, 2019.
2. Viekira XR Prescribing Information. North Chicago, IL: Abbvie Pharmaceuticals Corp; July 2018. Available at https://www.rxabbvie.com/. Accessed April 30, 2019.
3. 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 May 24, 2018. Available at: https://www.hcvguidelines.org/. Accessed April 30, 2019.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy converted to new template from "Viekira Pak, Viekira XR NATL 09.27.16.docx". Annual Review – added requirement for tx and cirrhosis status; added trial of Epclusa for those not a candidate for Harvoni; added re-direction to Epclusa if >12 week request for Harvoni; added pre- and post-liver transplant as candidates for tx per 2017 AASLD guideline.	06.17	11.17
Added redirection to Mavyret for FDA-approved indications and as an option in addition to Epclusa for Harvoni requests >12 weeks. Safety criteria were 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 to ensure that proper risk reduction measures are taking, though this is not specifically addressed in boxed warning.	09.05.17	11.17
3Q 2018 annual review: removed requirement for HBV verification; added age limit; removed requirement for documentation of treatment status since it does not change treatment duration; removed redirection to Epclusa or Mavyret if treatment duration is greater than 12 weeks since parity and redirections no longer shorten duration of tx; added requirement that prescribed regimen should be consistent with FDA or AASLD recommendations; expanded duration of tx required for COC from 30 days to three quarters of the full regimen; required verification of genotype for COC; reduced maximum approval duration from 24 weeks to 12 weeks per AASLD/IDSA September 2017 guidance; removed prior DAA failure and decompensated cirrhosis status from section III dx not allowed since other sections of the criteria already addresses this issue; references reviewed and updated.	05.22.18	08.18
Removed requirement for advanced fibrosis or other candidacy for therapy following approved clinical guidance; combined with and retired CP.CPA.EX.288 for HNAZ exchange lines of business.	09.03.18	
No clinically significant changes: revised preferencing from Harvoni, Epclusa, and Mavyret to Harvoni (Brand/AG) for 8 weeks only, Epclusa AG only, Mavyret, and Zepatier in line with previously approved clinical guidance.	01.07.19	
3Q 2019 annual review: no clinically significant changes; references reviewed and updated.	05.23.19	08.19

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 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.

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