Clinical Policy Title:	dasabuvir/ombitasvir/paritaprevir/ritonavir
Policy Number:	RxA.550
Drug(s) Applied:	Viekira XR®, Viekira Pak®
Original Policy Date:	01/2020
Last Review Date:	12/07/2020
Line of Business Policy Applies to:	All lines of business

Background

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.
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

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose	Reference
Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir (Viekira XR®, Viekira Pak®)	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/ ombitasvir 25 mg per day; dasabuvir 500 mg per day	1) FDA-approved labeling 2) AASLD-IDSA (updated May 2018)
Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir (Viekira XR®, Viekira Pak®)	Genotype 1b: Treatment-naïve or treatment-experienced with pegIFN/RBV with or without compensated cirrhosis	Viekira Pak®/XR® for 12 weeks	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)

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.

Dosage Forms

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.*

Clinical Policy

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

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® (*brand preferred over generic*) or Epclusa® (*brand preferred over generic)* unless 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 week*)

II. Continued Therapy Approval

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication via RxAdvance 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)*

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

AASLD: American Association for the Study of Liver Diseases	IDSA: Infectious Diseases Society of America
FDA: Food and Drug Administration	NS3/4A, NS5A/B: nonstructural protein
HBV: hepatitis B virus	PegIFN: pegylated interferon
HCV: hepatitis C virus	RBV: ribavirin
HIV: human immunodeficiency virus	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	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 12 weeks	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**	sofosbuvir 400 mg/ velpatasvir 100 mg (1 tablet) per day

Drug Name	Dosing Regimen	Maximum Dose
	One tablet PO QD for 12 weeks	
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	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 PO QD plus weight-based RBV for 16 weeks	One tablet (grazoprevir 100 mg/ elbasvir 50 mg) per day
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
  - Known hypersensitivity to ritonavir (e.g. toxic epidermal necrolysis, Stevens-Johnson syndrome)
- 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				
	NASA Inhibitor	Nucleotide Analog NSSB Polymerase Inhibitor	Non-Nucleoside NS5B Palm Polymerase Inhibitor	NS3/4A Protease Inhibitor (PI)	CYP3A Inhibitor
	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.

References

1. Viekira Pak Prescribing Information. North Chicago, IL: Abbvie Pharmaceuticals Corp; Dec 2019. Available at https://www.rxabbvie.com/. Accessed November 24, 2020.
2. Viekira XR Prescribing Information. North Chicago, IL: Abbvie Pharmaceuticals Corp; Dec 2019. Available at https://www.rxabbvie.com/. Accessed November 24, 2020.
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 August 27, 2020. Available at: https://www.hcvguidelines.org/. Accessed November 24, 2020.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Policy title table was updated. 2. Initial approval criteria I.A.6 updated to limit try and fail products to Epclusa and Harvoni and to reflect use of brand over generic due to rebates available. 3. Appendix B updated. 4. Appendix C updated to add new contraindication for hypersensitivity to ritonavir. 5. References were updated.	11/24/2020	12/07/2020