Clinical Policy Title:	dasabuvir/ombitasvir/paritaprevir/ritonavir
Policy Number:	RxA.550
Drug(s) Applied:	Viekira Pak®
Original Policy Date:	03/06/2020
Last Review Date:	10/19/2022
Line of Business Policy Applies to:	All lines of business

Background

Dasabuvir/paritaprevir/ritonavir/ombitasvir (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 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
dasabuvir/ombitasvir/ paritaprevir/ritonavir (Viekira Pak®)	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/ ombitasvir 25 mg per day/dasabuvir 500 mg per day
	Genotype 1b: Treatment-naïve or treatment-experienced with pegIFN/RBV with or without compensated cirrhosis	Viekira Pak® for 12 weeks*	

*The recommended oral dosage of Viekira Pak® is two ombitasvir, paritaprevir, ritonavir tablets once daily (in the morning) and one dasabuvir tablet twice daily (morning and evening).

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 2021 no longer recommends use of Viekira Pak® for the treatment of genotype 1a with compensated cirrhosis.
Hepatic Impairment Dosing: Use is contraindicated in patients with moderate to severe hepatic impairment (Child-Pugh Class B and C). In addition, the manufacturer recommends treatment be avoided in patients with decompensated liver disease.

Dosage Forms

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

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. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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 specialist or a liver transplant physician;
4. Age ≥ 18 years;
5. If cirrhosis is present, confirmation of Child-Pugh A status;
6. Member must use Epclusa® unless contraindicated or clinically significant adverse effects are experienced;*
   *Coadministration with omeprazole up to 20 mg is not considered acceptable medical justification for inability to use Epclusa
7. Life expectancy ≥ 12 months with HCV treatment;
8. Member agrees to participate in a medication adherence program including both of the following components (a and b):
   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;
9. 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;
10. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (see Section V Dosage and Administration for reference);
11. Dose does not exceed For Viekira Pak®: ombitasvir/paritaprevir/ritonavir 12.5 mg/75 mg/50 mg (2 tablets) once daily and dasabuvir 250mg (1 tablet) twice daily;

Approval Duration
Commercial: 3 months
Medicaid: 3 months
(*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. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy ;
   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. If request is for dose increase, dose does not exceed for Viekira Pak®: ombitasvir/paritaprevir/ritonavir 12.5 mg/75 mg/50 mg (2 tablets) once daily and dasabuvir 250mg (1 tablet) twice daily;

Approval Duration
Commercial: 3 months
Medicaid: 3 months
(*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
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Maximum Dose
sofosbuvir/ velpatasvir (Epclusa®)	Treatment-naïve or treatment-experienced with pegIFN/RBV with or without compensated cirrhosis: **Genotype 1** One tablet orally once daily for 12 weeks	sofosbuvir 400 mg/ velpatasvir 100 mg (1 tablet) per day

Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only.

APPENDIX C: Contraindications*/Boxed Warnings
- Contraindication(s):
  - Patients with moderate to severe hepatic impairment (Child-Pugh B and C) due to risk of potential toxicity.

- If Viekira Pak® 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 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)

*Contraindications listed reflect direct statements made in the manufacturer's package insert; for additional uses, warnings, and precautions, please refer to clinical guidelines.

- 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
Epclusa*	velpatasvir	sofosbuvir			
Harvoni*	ledipasvir	Sofosbuvir			
Mavyret*	pibrentasvir			glecaprevir	
Sovaldi		sofosbuvir			
Viekira PAK*	ombitasvir		dasabuvir	paritaprevir	ritonavir
Vosevi*	velpatasvir	sofosbuvir		voxilaprevir	
Zepatier*	elbasvir			grazoprevir	

*Combination drugs

APPENDIX E: General Information

- Acceptable medical justification for inability to use Epclusa:
  - 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:
  - 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
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 September 19, 2022.
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 September 29, 2021. Available at: https://www.hcvguidelines.org/. Accessed September 19, 2022.
3. CDC. Hepatitis C Q&As for health professionals. Last updated August 7, 2020. Available at: https://www.cdc.gov/hepatitis/hcv/hcvfaq.htm. Accessed September 19, 2022.
4. Clinical Pharmacology [database online] powered by ClinicalKey. Tampa, FL: Elsevier, 2022. Accessed with subscription at: http://www.clinicalkey.com. Accessed September 19, 2022.
5. Viekira Pak®, Lexi-Drug. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed with subscription at: http://online.lexi.com. Accessed September 19, 2022.

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	11/24/2020	12/07/2020

rebates available. 3. Appendix B updated. 4. Appendix C updated to add new contraindication for hypersensitivity to ritonavir. 5. References were updated.		
Policy was reviewed: 1. Dosing information was updated to remove reference table from there. 2. Dosing information was updated to include new indication Genotype 1a, with compensated cirrhosis. 3. Dosing information was updated to include Hepatic impairment dosing. 4. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 5. Approval durations were updated from 12 weeks to 3 months. 6. Continued Therapy Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 7. Therapeutic Alternative verbiage was rephrased to “Below are suggested therapeutic alternatives based on clinical guidance..”. 8. Appendix B was updated to remove generics "grazoprevir/ elbasvir, and glecaprevir/ pibrentasvir", as these were not available. 9. Statement about drug listing format in Appendix B is updated to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only. 10. Viekira XR is discontinued. Information pertaining to it removed throughout the policy. 11. References were reviewed and updated.	10/02/2021	12/07/2021

Policy was reviewed: 1. Dosing Information, Indication: Updated to remove indication Genotype 1a, with compensated cirrhosis. 2. Dosing Information, Dosing Regimen, dasabuvir/ombitasvir/ paritaprevir/ritonavir(Viekira Pak®): Updated to remove dosing information for indication Genotype 1a, with compensated cirrhosis. 3. Dosing Information, Dosing Regimen, Viekira Pak®: Updated to include specific information regarding dose, for indication HCV. 4. Initial Approval Criteria, I.A.3: Updated prescriber criteria from Prescribed by or in consultation with a gastroenterologist, hepatologist or infectious disease physician to Prescribed by or in consultation with a gastroenterologist, hepatologist or infectious disease specialist or a liver transplant physician. 5. Initial Approval Criteria, I.A.6: Updated trial and failure criteria from Member must use Harvoni® (brand preferred over generic) or Epclusa® (brand preferred over generic) unless contraindicated or clinically significant adverse effects are experienced to Member must use Epclusa® unless contraindicated or clinically significant adverse effects are experienced. *Coadministration with omeprazole up to 20 mg is not considered acceptable medical justification for inability to use Epclusa. 6. Initial Approval Criteria, 1.A.7: Updated to include new criteria pertaining to indication Chronic Hepatitis C Infection, Life expectancy ≥ 12 months with HCV treatment.	09/19/2022	10/19/2022

7. Initial Approval Criteria, 1.A.8: Updated to include new Medication adherence program criteria 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; 8. Initial Approval Criteria, 1.A.9: Updated to include new dosing criteria 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. 9. Statement about provider sample ''The provision of provider samples does not guarantee coverage…" was added to Clinical Policy. 10. Continued Therapy Approval, II.A.1.b.i: Updated documentation criteria from Documentation supports that member is currently receiving Viekira Pak® for chronic HCV infection and has recently completed at least three quarters of the full regimen with Viekira Pak® to 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®. 11. Appendix B, Drug Name: Updated to remove therapeutic alternatives: a. sofosbuvir/ledipasvir (Harvoni®), b. Mavyret®, c. Zepatier®. 12. Appendix D: Updated to remove drugs daclatasvir, Olysio, simeprevir, Technivie*, ombitasvir, paritaprevir, ritonavir under Direct-Acting Antivirals for Treatment of HCV infection.		

13. Appendix E, General Information: Updated to include new information regarding Acceptable and Unacceptable medical justification for inability to use Epclusa. 14. References were reviewed and updated.		