

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

Reference Number: LA.PHAR.278

Effective Date: 09/16

Last Review Date: 07/18

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;
Chart note documentation and copies of lab results are required
3. Age \geq 18 years;
4. If cirrhosis is present, confirmation of Child-Pugh A status;
5. Member is contraindicated to treatment with Mavyret due to current treatment with efavirenz or atazanavir;
**See Appendix F for additional details on acceptable contraindications*
6. Life expectancy \geq 12 months with HCV treatment;
7. Documentation required that member is not actively participating in alcohol and/or illicit IV drugs use, if applicable;
8. Advanced liver disease defined as (a,b or c):
 - a. Advanced fibrosis indicated by i, ii, or iii:

- i. Liver biopsy showing a METAVIR score of F3 or equivalent (Knodell, Scheuer, Batts-Ludwig – F3; Ishak – F4/5);
 - ii. One serologic test showing an equivalent score to METAVIR F3
 - iii. One radiologic test showing an equivalent score to METAVIR F3 per Appendix C;
 - b. Cirrhosis indicated by i, ii, iii, iv or v:
 - i. Hepatocellular carcinoma (HCC) 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. One serologic test showing an equivalent score to METAVIR F4 per Appendix C;
 - iv. One radiologic test showing an equivalent score to METAVIR F4 per Appendix C;
 - v. Other radiologic test showing evidence of cirrhosis (e.g., portal hypertension)
 - c. If member is HIV/HCV co-infected, there shall be no METAVIR score requirements.
9. Prescribed regimen is consistent with an FDA or AASLD-IDSAs recommended regimen (*see Section V Dosage and Administration for reference*);
10. 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;
11. 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 a total of 12 weeks*

(*Approved duration should be consistent with a regimen in Section V Dosage and Administration; The AASLD/IDSAs 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.PMN.53 for Medicaid.

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 60 days of treatment with Viekira XR or Viekira Pak;
 - ii. Confirmed HCV genotype is 1;
- 2. Member is responding positively to therapy (e.g. decreased HCV RNA level, no unacceptable toxicity);
- 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.PMN.53 for Medicaid.

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

| | |
|---|--|
| AASLD: American Association for the Study of Liver Diseases | IDSA: Infectious Diseases Society of America |
| APRI: AST to platelet ratio | IQR: interquartile range |
| FDA: Food and Drug Administration | MRE: magnetic resonance elastography |
| FIB-4: Fibrosis-4 index | NS3/4A, NS5A/B: nonstructural protein |
| HBV: hepatitis B virus | PegIFN: pegylated interferon |
| HCC: hepatocellular carcinoma | RBV: ribavirin |
| HCV: hepatitis C virus | RNA: ribonucleic acid |
| HIV: human immunodeficiency virus | |

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 |
|------------------|---------------------------------------|---|
| Mavyret™ | Treatment-naïve: Genotype 1 | Mavyret: glecaprevir 300 mg/pibrentasvir |

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|--|---|---|
| (glecaprevir/ pibrentasvir) | Without cirrhosis: Three tablets PO QD for 8 weeks With compensated cirrhosis: Three tablets PO QD for 12 weeks | 120 mg (3 tablets) per day |
| Mavyret [™] (glecaprevir/ pibrentasvir) | Treatment-experienced with IFN/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 |

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

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

Appendix D: 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 E: 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 F: 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.
- Acceptable medical justification for inability to use Mavyret (preferred product):
 - Severe hepatic disease (Child-Pugh C): use of Mavyret is not recommended due to higher exposures of glecaprevir and pibrentasvir.
 - Moderate hepatic disease (Child-Pugh B): although not an absolute contraindication, use of Mavyret is not recommended in patients with moderate hepatic disease (Child-Pugh B) due to lack of safety and efficacy data.
 - Following administration of Mavyret in HCV infected subjects with *compensated* cirrhosis (Child-Pugh A), exposure of glecaprevir was

- approximately 2-fold and pibrentasvir exposure was similar to non-cirrhotic *HCV infected* subjects.
- At the clinical dose, compared to *non-HCV infected* subjects with *normal hepatic function*, glecaprevir AUC was 100% higher in Child-Pugh B subjects, and increased to 11-fold in Child-Pugh C subjects. Pibrentasvir AUC was 26% higher in Child-Pugh B subjects, and 114% higher in Child-Pugh C subjects.
 - Drug-drug interactions with one or more the following agents:
 - Atazanavir
 - Efavirenz
 - Unacceptable medical justification for inability to use Mavyret (preferred product):
 - Black Box Warning (BBW): currently or previously infected with hepatitis B virus. This BBW is not unique to Mavyret, and it applies across the entire therapeutic class of direct-acting antivirals for treatment of HCV infection. Therefore it is not a valid clinical reason not to use Mavyret.
 - Concurrent anticoagulant therapy: Fluctuations in International Normalized Ratio (INR) have been observed in warfarin recipients who were also receiving treatment for HCV infections. This BBW is not unique to Mavyret, and it applies across the entire therapeutic class of direct-acting antivirals for treatment of HCV infection. Although caution is advised when using Mavyret while receiving concurrent anticoagulant therapy, specifically warfarin, this is not an absolute contraindication as long as patient is adequately monitored and educated during therapy.
 - Drug-drug interactions with one or more of the following agents:
 - Rifampin, carbamazepine, or St. John’s wort:
 - These drug-drug interactions are not unique to Mavyret, and they apply across the entire therapeutic class of direct-acting antivirals for treatment of HCV infection

V. nDosage and Administration

| Indication | Dosing Regimen | Maximum Dose | Reference |
|---|---|---|--|
| Genotype 1a: Treatment-naïve 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 September 2017) |
| 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 September 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 <i>*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.</i> |
| Paritaprevir/ritonavir/ombitasvir/ dasabuvir (Viekira XR) | Extended-release tablets: dasabuvir 200 mg, ombitasvir 8.33 mg, paritaprevir 50 mg, and ritonavir 33.33 mg <i>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.</i> |

VII. References

1. Viekira Pak Prescribing Information. North Chicago, IL: Abbvie Pharmaceuticals Corp; November 2017. Available at www.viekira.com. Accessed May 1, 2018.
2. Viekira XR Prescribing Information. North Chicago, IL: Abbvie Pharmaceuticals Corp; November 2017. Available at www.viekira.com. Accessed May 1, 2018.
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 September 21, 2017. Available at: <https://www.hcvguidelines.org/>. Accessed May 1, 2018.
4. Platt L, Easterbrook P, Gower E, et al. Prevalence and burden of HCV co-infection in people living with HIV: a global systematic review and meta-analysis. *Lancet Infect Dis* 2016;16:797-808. <http://dx.doi.org/10.1016/>
5. Centers for Disease Control and Prevention. HIV and viral hepatitis: fact sheet. June 2016. Available at: <https://www.cdc.gov/hiv/pdf/library/factsheets/hiv-viral-hepatitis.pdf>. Accessed March 13, 2018.
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 May 1, 2018.

9. Hepatitis C Virus (HCV) FibroTest-ActiTest Panel. Nichols Institute/Quest Diagnostics. Available at http://education.questdiagnostics.com/physician_landing_page. 2017. Accessed May 1, 2018.
 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 May 1, 2018.
- 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

| Reviews, Revisions, and Approvals | Date | Approval Date |
|---|-------|---------------|
| <p>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).</p> <p>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.</p> | 08/16 | 09/16 |
| <p>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.</p> | 08/17 | 09/17 |

| Reviews, Revisions, and Approvals | Date | Approval Date |
|--|------|---------------|
| Due to State requirements, removed prescriber restrictions regarding who can prescribe Hepatitis C DAA agents; Removed the abstinence period of 6 months and added documentation required that member is not actively participating in alcohol and/or illicit IV drugs use,; Added statement for NO Fibrosis score required for HIV/HCV co-infected members Changed language to one serologic test OR one radiologic test from one serologic test and one radiologic test | 5/18 | 5/18 |
| 3Q 2018 annual review: removed requirement for HBV verification; removed requirement to check for ART for HCV/HIV co-infection; expanded duration of tx required for COC from 30 days 60 days; required verification of genotype for COC; removed conditional requirement for RBV CI; reduced maximum approval duration from 24 weeks to 12 weeks per AASLD/IDSA September 2017 guidance; references reviewed and updated. | 7/18 | 07/18 |

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.

©2016 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene[®] and Centene Corporation[®] are registered trademarks exclusively owned by Centene Corporation.