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

Reference Number: GA.PMN.12
Effective Date: 12/16
Last Review Date: 7/2024 Revision Log
Line of Business: Medicaid

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

Description
Dasabuvir/paritaprevir/ritonavir/ombitasvir (Viekira Pak™) is a combination of ombitasvir, a hepatitis C virus (HCV) 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(s)
Viekira Pak is 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.

Policy/Criteria
It is the policy of health plans affiliated with Centene Corporation® that 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. Hepatitis C Infection (must meet all)**:**
1. Diagnosis of chronic hepatitis C virus (HCV) infection as evidenced by detectable serum HCV ribonucleic acid (RNA) levels by quantitative assay in the last 6 months;
2. Age ≥ 18 years;
3. Confirmed HCV genotype is 1;
   *Chart note documentation and copies of labs results are required
4. Member must use **sofosvubir/velpatasvir (Epclusa® *authorized generic*) or Mavyret®**, unless both are contraindicated or clinically significant adverse effects are experienced; (*see Appendix E*);*
   **Coadministration with omeprazole up to 20 mg is not considered acceptable medical justification for inability to use Epclusa*
5. If cirrhosis is present, confirmation of Child-Pugh A status;
6. Life expectancy ≥ 12 months with HCV treatment;
7. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (*in Section III Dosage and Administration)*;

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 E*);
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;
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 in Section III Dosage and Administration)*

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Member must use **sofosvubir/velpatasvir (Epclusa *authorized generic*)** or **Mavyret**, if applicable for the requested indication, unless clinically significant adverse effects are experienced or both are contraindicated;
2. One of the following (a or b):
    a. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (i or ii):

i. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
ii. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or

b. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 2a above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

II. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AASLD: American Association for the Study of Liver Diseases
APRI: AST to platelet ratio
CTP: Child Turcotte Pugh
CrCl: creatinine clearance
FDA: Food and Drug Administration
FIB-4: Fibrosis-4 index
HCC: hepatocellular carcinoma
HCV: hepatitis C virus
IDSA: Infectious Diseases Society of America
MRE: magnetic resonance elastography
NS3/4A, NS5A/B: nonstructural protein
Peg-IFN: pegylated interferon
PI: protease inhibitor
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
Epclusa® (sofosbuvir/ velpatasvir)	Treatment-naïve or treatment-experienced with pegIFN/RBV without cirrhosis or with 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: **Genotype 1** Without cirrhosis or with compensated cirrhosis: Three tablets PO QD for 8 weeks	Mavyret: glecaprevir 300 mg/pibrentasvir 120 mg (3 tablets) per day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Mavyret® (glecaprevir/ pibrentasvir)	Treatment-experienced with IFN/pegIFN + RBV +/- sofosbuvir: **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

Theraputic alternatives are listed as Brand Name® (generic) when the drug is a 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 Pak is contraindicated in:
  - Patients with moderate to severe hepatic impairment (Child-Pugh B and C) due to risk of potential toxicity
  - If 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
    - Moderate or strong inducers of CYP3A and strong inducers of CYP2C8 and may lead to reduced efficacy of Viekira Pak
    - Strong inhibitors of CYP2C8 and may increase dasabuvir plasma concentrations and the risk of QT prolongation
  - Patients with known hypersensitivity to ritonavir (e.g., toxic epidermal necrolysis (TEN) or 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				
	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	
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 Mavyret (preferred product):
  - Drug-drug interactions with atazanavir
- Acceptable medical justification for inability to use Epclusa (preferred product):
  - 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 (preferred product):
  - 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 (HBV) Reactivation 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.

Appendix F: Incomplete Adherence and AASLD-IDSA Recommended Management of Treatment Interruptions

- There are minimal data regarding the outcome of patients who have incomplete adherence to DAA therapy or the threshold level of adherence below which the incidence of sustained virologic response at 12 weeks (SVR12) is significantly reduced. In general, a treatment interruption of < 7 days is unlikely to impact SVR12.
- There are few data on which to base recommendations regarding how to manage patients who have discontinued DAAs for several days to weeks. The below recommendations are applicable to treatment-naive patients with HCV, without cirrhosis or with compensated cirrhosis*, receiving either Mavyret or Epclusa*. Patients with prior DAA treatment, or receiving other DAA treatment regimens, or other populations (e.g., patients who are posttransplant or have decompensated cirrhosis) should be managed in consultation with an expert.
    - Interruptions during the first 28 days of DAA therapy:
        - If missed ≤ 7 days, restart DAA therapy immediately and complete therapy for originally planned duration (8 or 12 weeks).
        - If missed ≥ 8 days, restart DAA therapy immediately and obtain HCV RNA test as soon as possible. If HCV RNA is negative, complete originally planned DAA treatment course (8 or 12 weeks). Recommendation to extend DAA treatment for an additional 4 weeks for patients with genotype 3 and/or cirrhosis. If HCV RNA is positive or not obtained, extend DAA treatment for an additional 4 weeks.
    - Interruptions after receiving ≥ 28 days of DAA therapy:
        - If missed ≤ 7 days, restart DAA therapy immediately and complete therapy for originally planned duration (8 or 12 weeks).
        - If missed 8-20 consecutive days, restart DAA therapy immediately and obtain HCV RNA test as soon as possible. If HCV RNA is negative, complete originally planned DAA treatment course (8 or 12 weeks). Recommendation to extend DAA treatment for an additional 4 weeks for patients with genotype 3 and/or cirrhosis. If HCV RNA is positive or not obtained, stop treatment and retreat according to the recommendations in the AASLD-IDSA Retreatment Section.
        - If missed ≥ 21 consecutive days, stop DAA treatment and assess for SVR12. If SVR12 not achieved, retreat according to the recommendations in the AASLD-IDSA Retreatment Section.

III. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose	Reference
Genotype 1a: Treatment-naive or interferon-experienced without cirrhosis	Viekira Pak plus weight-based RBV for 12 weeks	Viekira Pak: paritaprevir 150 mg /ritonavir 100 mg/ ombitasvir 25 mg per day; dasabuvir 500 mg per day	FDA-approved labeling
Genotype 1a: Treatment-naïve or interferon-experienced with compensated cirrhosis	Viekira Pak plus weight-based RBV for 24 weeks* *In some patients, the treatment duration may be reduced to 12 weeks based on patient's prior treatment history		
Genotype 1b: Treatment-naïve or interferon-experienced with or without compensated cirrhosis	Viekira Pak for 12 weeks		

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 for the treatment of genotype 1a with compensated cirrhosis.

IV. 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.*

V. References

1. Viekira Pak Prescribing Information. North Chicago, IL: Abbvie Pharmaceuticals Corp; December 2019. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/206619s020lbl.pdf /. Accessed May 8, 2024.
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 December 19, 2023. Available at: https://www.hcvguidelines.org/. Accessed May 20, 2024.
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 May 5, 2023.

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	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	9/17
Annual review. No changes made.	3/18	3/18
Changed current Georgia policy templates to corporate standard templates for drug coverage criteria to meet corporate compliance. Changes/revisions included; new formatting, font size, use of standard policy language for each section of policy, and rearranged order of certain steps in criteria and sections. Added new preferred treatment tables that includes dosage and frequency based on genotype for Mavyret. Removed background sections.	2/21/19	2/19

Reviews, Revisions, and Approvals	Date	Approval Date
Updated general information and contraindication section to be consistent with corporate HCV policies.		
Annual Review. Removed Viekira XR from policy as it was removed from the market 5/18. In the initial approval criteria, changed RNA detectable period from "over a 6 month period" to "in the last 6 months" for infection diagnosis.	10/19	10/19
RT4: updated Mavyret dosing recommendations to 8 weeks total duration of therapy for treatment-naïve HCV with compensated cirrhosis across all genotypes (1-6). Added preferencing for AG Epclusa or Mavyret; removed redirection to Mavyret based on contraindications criteria; Removed Appendix D for Metavir scoring. Removed dosing for Mavyret treatment-naïve. Updated order of all other Appendices. Updated references.	4/2020	4/2020
References reviewed and updated.	7/2020	7/2020
Annual review. Added Mayvret and Vosevi to Appendix D-Direct Acting Antivirals for Treatment of HCV infection and removed Olysio, Technivie, and Viekira XR as these were previously removed from the market. Updated Appendix B: Therapeutic Alternatives dosing regimens. Changed Centene Logo to PSHP Logo. References reviewed and updated.	4/2021	4/2021
Included reference to Appendix E with addition of contraindications that would warrant bypassing preferred agents; references reviewed and updated.	7/2021	7/2021
3Q 2022 annual review. Added omeprazole coadministration as unacceptable rationale for not using preferred Epclusa in Appendix E; references reviewed and updated.	7/2022	7/2022
Added omeprazole coadministration as unacceptable rationale for not using preferred Epclusa to criteria. Minor font updates.	10/2022	10/2022
Template changes applied to other diagnoses/indications.	1/2023	1/2023
3Q 2023 annual review: Added preferred redirections to other diagnoses/indications section; references reviewed and updated.	7/2023	7/2023
3Q 2024 annual review: removed qualifier of "chronic" from HCV criteria as AASLD-IDSA recommends treatment of both acute and chronic HCV; removed "preferred" from Epclusa authorized generic redirection; added Appendix F for guidance on incomplete adherence and AASLD-IDSA recommended management of treatment interruptions; references reviewed and updated.	7/2024	7/2024

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.