Clinical Policy: Ombitasvir/Paritaprevir/Ritonavir (Technivie)

Reference Number: CP.CPA.287
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

Ombitasvir/paritaprevir/ritonavir (Technivie™) is a combination fixed-dose oral tablet formulation consisting of an NS5A inhibitor (ombitasvir), NS3/4A protease inhibitor (paritaprevir), and CYP3A inhibitor (ritonavir).

FDA Approved Indication(s)

Technivie is indicated in combination with ribavirin (RBV) for the treatment of patients with genotype 4 chronic hepatitis C virus (HCV) infection without cirrhosis or with compensated cirrhosis.

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 Technivie is **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 4;
   **Chart note documentation and copies of lab results are required*
3. If cirrhosis is present, confirmation of Child-Pugh A status;
4. Prescribed by or in consultation with a gastroenterologist, hepatologist or infectious disease physician;
5. Age ≥ 18 years;
6. Member must use sofosbuvir/velpatasvir (Epclusa®) (*authorized generic preferred*), Mavyret™, or Zepatier® unless all are contraindicated or clinically significant adverse effects are experienced;
7. Prescribed in combination with RBV;
8. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (*see Section V Dosage and Administration for reference)*;
9. Dose does not exceed Techinvie (ombitasvir/paritaprevir/ritonavir) 25 mg/150 mg/100 mg (2 tablets) per day.

Approval duration: 12 weeks*

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

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 Technivie for chronic HCV infection and has recently completed at least three quarters of the full regimen with Technivie;
      ii. Confirmed HCV genotype is 4;
2. Member is responding positively to therapy;
3. Dose does not exceed Technivie (ombitasvir/paritaprevir/ritonavir) 25 mg/150 mg/100 mg (2 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)*

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 or evidence of coverage documents;

B. Patients who have failed to respond to previous protease inhibitor (Olysio, Victrelis, Viekira Pak) based therapy;

C. Patients with decompensated cirrhosis (Child-Pugh Class B or C).

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
Epclusa® (sofosbuvir/ velpatasvir)	Treatment-naïve or treatment-experienced with pegIFN/RBV with or without compensated cirrhosis: **Genotype 4** One tablet PO QD for 12 weeks	Epclusa: sofosbuvir 400 mg/ velpatasvir 100 mg (1 tablet) per day
Mavyret™ (glecaprevir/ pibrentasvir)	Treatment-naïve: **Genotype 4** 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
Mavyret™ (glecaprevir/ pibrentasvir)	Treatment-experienced with IFN/pegIFN + RBV: **Genotype 4** 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 4:** Treatment-naïve 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 4:** PegIFN/RBV-experienced with or without compensated cirrhosis with virologic relapse/failure Virologic relapse after prior pegIFN/RBV therapy: One tablet PO QD for 12 weeks Virologic failure while on pegIFN/RBV therapy:	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	

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):
  - In patients with moderate to severe hepatic impairment (Child-Pugh B and C) due to risk of potential toxicity
  - 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.
  - With drugs that are moderate or strong inducers of CYP3A and may lead to reduced efficacy of Technivie.
  - In patients with known hypersensitivity to ritonavir (e.g., toxic epidermal necrolysis (TEN) or Stevens-Johnson syndrome)
  - The contraindications to RBV also apply to this combination regimen. Refer to the RBV prescribing information for a list of contraindications for RBV.
- 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 4: Treatment-naïve or treatment- experienced with pegIFN/RBV with or without compensated cirrhosis	Technivie 2 tablets PO qAM plus weight-based RBV for 12 weeks	Two tablets (paritaprevir 150 mg, ritonavir 100 mg, ombitasvir 25 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.

VI. Product Availability

Tablet: paritaprevir 75 mg, ritonavir 50 mg, ombitasvir 12.5 mg

VII. References

1. Technivie Prescribing Information. North Chicago, IL: AbbVie, Inc.; July 2018. Available at http://www.rxabbvie.com/pdf/technivie_pi.pdf. Accessed April 30, 2019.
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 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 "Technivie NATL 07.22.16.docx" and "Technivie Envolve PAC 04.11.17_ver2.docx". Annual Review – added requirement of cirrhosis status; added trial of Epclusa for those not a candidate for Harvoni; added re-direction to Epclusa if >12 week request for Harvoni; clarified what chart notes and labs (GT) and tx-status is required.	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; removed requirement for documentation of treatment status since it does not change treatment duration; added age limit; added requirement that prescribed regimen should be consistent with FDA or AASLD recommendations; removed redirection to Epclusa or Mavyret if treatment duration is greater than 12 weeks since parity and redirections no longer shorten duration of tx; expanded duration of tx required for COC from 30 days to three quarters of the full regimen; required verification of genotype for COC; 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.287 for HNAZ exchange lines of business.	09.03.18	
No clinically significant changes: revised preferencing from Harvoni, Epclusa, and Mavyret to 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.	05.22.19	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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