Clinical Policy: Ombitasvir/Paritaprevir/Ritonavir (Technivie)

Reference Number: OH.PHAR.PPA.07
Effective Date: 07/17
Last Review Date: 09/17
Line of Business: Medicaid

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

Technivie is indicated in combination with ribavirin 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 (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 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 multiple detectable HCV RNA (ribonucleic acid) levels in the last 6 months;
2. Confirmed HCV genotype is 4;
3. Prescribed by or in consultation with a gastroenterologist, hepatologist, or infectious disease specialist;
4. Age ≥ 18 years;
5. Member has no cirrhosis or compensated cirrhosis;
6. Life expectancy ≥ 12 months with HCV treatment;
7. Documented sobriety from alcohol and illicit IV drugs for ≥ 6 months prior to starting therapy, if applicable;
8. Moderate or Advanced liver disease defined as a or b:
   a. Moderate or Advanced fibrosis indicated by i or ii:
      i. Liver biopsy showing a METAVIR score of F2 or equivalent (Knodell, Scheuer, Batts-Ludwig – F2; Ishak – F3);
      ii. One serologic test and one radiologic test showing an equivalent score to METAVIR F2 per Appendix C;
   b. Cirrhosis indicated by i, ii or iii:
      i. Hepatocellular carcinoma (HCC) - and the HCC is 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. Both of the following:
a) One serologic test showing an equivalent score to METAVIR F4 per Appendix C;
b) One radiologic test showing an equivalent score to METAVIR F4 per Appendix C or other radiologic test showing evidence of cirrhosis (e.g., portal hypertension);

9. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (*see Section V Dosage and Administration for reference)*;
10. If member is without cirrhosis or with compensated cirrhosis (Child-Pugh A): contraindication or intolerance to Mavyret;
11. Member agrees to participate in a medication adherence program meeting 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;
12. If HCV/HIV-1 (human immunodeficiency virus type-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;
13. 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 B*);
14. At the time of request, member has none of the following contraindications:
    a. If prescribed with ribavirin, at the time of request, member has none of the following contraindications:
        i. Pregnancy;
        ii. For Rebetol: creatinine clearance < 50 mL/min;
15. Dose does not exceed ombitasvir/paritaprevir/ritonavir 25 mg/15 0mg/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 CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Approval

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

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Technivie for chronic hepatitis C virus infection and has received this medication for at least 30 days;

2. 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;
3. Member is responding positively to therapy (e.g. decreased HCV RNA level, no unacceptable toxicity);
4. Dose does not exceed ombitasvir/paritaprevir/ritonavir 25mg/150mg/100mg (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 CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 Key

ALT: alanine aminotransferase
APRI: AST to platelet ratio
AASLD: American Association for the Study of Liver Diseases
FIB-4: Fibrosis-4 index
HBeAg: hepatitis B virus envelope antigen
HBV: hepatitis B virus
HCC: hepatocellular carcinoma
HCV: hepatitis C virus
HIV: human immunodeficiency virus
IDSA: Infectious Diseases Society of America
MRE: magnetic resonance elastography
NS3/4A, NS5A/B: nonstructural protein
RBV: ribavirin

Appendix B: General Information

- Hepatitis B Reactivation is a black box warning for all direct-acting antiviral drugs for the treatment of HCV. The provider must provide either:
  - Documentation of absence of concurrent HBV infection as evidenced by laboratory values showing absence of hepatitis B virus envelope antigen (HBeAg) and HBV DNA;
  - Documentation that HBV co-infected patient may not be candidates for therapy as evidenced by one of the following:
    - Absence of HBeAg, HBV DNA less than 2,000 international units/mL, and alanine aminotransferase (ALT) level within 1 to 2 times the upper limit of normal;
    - HBeAg-positive and HBV DNA greater than 1,000,000 international units/mL and ALT level within 1 to 2 times the upper limit of normal;

  - Documentation that concurrent HBV infection is being treated (e.g., tenofovir alafenamide, adefovir, entecavir), unless contraindicated or clinically significant adverse effects are experienced
- The 2016 AASLD/IDSA treatment guideline for HBV consider ALT levels <30 U/L for men and <19 U/L for women as upper limits of normal.
- The 2016 AASLD/IDSA treatment guideline for HBV recommend adults with compensated cirrhosis, even with low levels of viremia (<2,000 IU/mL) be treated with antiviral therapy to reduce the risk of decompensation, regardless of ALT level. The recommendation extends to adults with decompensated cirrhosis be treated with antiviral therapy indefinitely regardless of HBV DNA level, HBeAg status, or ALT level to decrease the risk of worsening liver-related complications.

Appendix C: Approximate Scoring Equivalencies using METAVIR F2/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
Moderate fibrosis	0.48 - 0.58	≥42	0.7 – 1.4	> 3.25	≥7.0	>3.2	F2	F3
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 F2 is equivalent to Knodell, Scheuer, and Batts-Ludwig F2 and Ishak F3
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 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				

Brand Name	Drug Class				
	NS5A Inhibitor	Nucleotide Analog NS5B Polymerase Inhibitor	Non-Nucleoside NS5B Palm Polymerase Inhibitor	NS3/4A Protease Inhibitor (PI)	CYP3A Inhibitor
Epclusa*	Velpatasvir	Sofosbuvir			
Harvoni*	Ledipasvir	Sofosbuvir			
Olysio				Simeprevir	
Sovaldi		Sofosbuvir			
Technivie*	Ombitasvir			Paritaprevir	Ritonavir
Viekira XR/PAK*	Ombitasvir		Dasabuvir	Paritaprevir	Ritonavir
Zepatier*	Elbasvir			Grazoprevir	

*Combination drugs

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose	Reference
Genotype 4: Treatment-naïve or treatment-experienced with pegylated interferon / ribavirin with or without compensated cirrhosis	Technivie 2 tablets PO qAM plus weight-based ribavirin For 12 weeks	Technivie (paritaprevir 150 mg, ritonavir 100 mg, ombitasvir 25 mg): 2 tablets per day	1) FDA-approved labeling 2) AASLD-IDSA (updated April, 2017)

VI. Product Availability

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

VII. References

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9. Bruix J and Sherman M. Management of hepatocellular carcinoma: An update. AASLD Practice Guideline. *Hepatology.* 2011; 53(3): 1020-22.
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Reviews, Revisions, and Approvals	Date	Approval Date
New policy created, split from CP.PHAR.17 Hep 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" consistent with the regimen tables; 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. Criteria added excluding post-liver transplantation unless regimens specifically designate. Dosing regimens are presented in Appendix D and E per AASLD guidelines and FDA-approved indications. The initial approval is shortened to 8 weeks.	08/16	09/16
Partial revision to add new FDA labeled indication: HCV genotype 4 infection with compensated cirrhosis (Appendix D). Policy converted to new template. Max dose added to criteria. Approval duration lengthened to 12 weeks; renewal criteria deleted. Added "+RBV" to the treatment-naïve regimen per AASLD-IDSA guidelines (Appendix E). PI updated. Added renewal criteria.	04/17	

Reviews, Revisions, and Approvals	Date	Approval Date
Added requirement for prevention of HBV reactivation. Deleted total in initial approval duration for consistency; consolidated appendix D and E into dosing and administration in section V; deleted adherence requirement in continued therapy, 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 to ensure that proper risk reduction measures are taken.	08/17	09/17

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.