Clinical Policy: Ombitasvir/Paritaprevir/Ritonavir (Technivie)

Reference Number: GA.PMN.14
Product: Medicaid
Effective Date: 12/16
Last Review Date: 3/18 Revision Log

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

Description
The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for ombitasvir/paritaprevir/ritonavir (Technivie®).

Policy/Criteria
It is the policy of health plans affiliated with Centene Corporation® that Technivie 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. Chronic Hepatitis C Infection (must meet all)**:**
1. Age ≥ 18 years;
2. Diagnosis of chronic hepatitis C virus (HCV) infection as evidenced by detectable HCV RNA (ribonucleic acid) levels over a six-month period;
3. Confirmed HCV genotype is 4;
4. Life expectancy ≥ 12 months with HCV treatment;
5. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (*see Appendix D and E for reference)*;
6. If member is without cirrhosis or with compensated cirrhosis (Child-Pugh A): Mavyret is preferred unless contraindication or intolerance
7. 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 F*);
8. 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;
9. Dose does not exceed ombitasvir/paritaprevir/ritonavir 25 mg/150 mg/100 mg (2 tablets) per day.
10. 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 CYP3A for clearance for which elevated plasma concentrations are associated with serious and/or life-threatening events, and moderate or strong inducers of CYP3A which may lead to

reduced efficacy of Technavie as follows: alfuzosin HCL, colchicine, ranolazine, dronedarone, carbamazepine, phenytoin, phenobarbital, 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 (PAH); 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 12 weeks*
*(*Approved duration should be consistent with a regimen in Appendix D or E)*

B. Other diagnoses/indications: Refer to CP.PHAR.57 - Global Biopharm Policy.

Background
Description/Mechanism of Action:
Technivie is a fixed-dose combination tablet containing ombitasvir, paritaprevir, and ritonavir for oral administration. Ombitasvir, paritaprevir, ritonavir fixed dose combination tablet includes a hepatitis C virus NS5A inhibitor (ombitasvir), a hepatitis C virus NS3/4A protease inhibitor (paritaprevir), and a CYP3A inhibitor (ritonavir) that inhibits CYP3A mediated metabolism of paritaprevir, thereby providing increased plasma concentration of paritaprevir.

Technivie Formulations
Tablet, Oral:
Technivie: Ombitasvir, paritaprevir and ritonavir film-coated tablets are co-formulated immediate release tablets. The strength for the tablet is 12.5 mg ombitasvir, 75 mg paritaprevir, 50 mg ritonavir.

Ribavirin Formulations
Capsule, Oral:
Rebetol: 200 mg
Ribasphere: 200 mg
Generic: 200 mg
Solution, Oral:
Rebetol: 40 mg/mL (100 mL)
Tablet, Oral:
Copegus: 200 mg
Moderiba (includes dose packs): 200 mg, 400 mg, 600 mg
Ribasphere: 200 mg, 400 mg, 600 mg

Ribasphere RibaPak (dose packs): 200 mg, 400 mg, 600 mg
Generic: 200 mg

FDA Approved Indications:
Technivie is a combination fixed-dose oral tablet formulation / NS5A inhibitor/NS3/4A protease inhibitor/CYP3A inhibitor indicated in combination with ribavirin for:

- Treatment of patients with genotype 4 chronic HCV infection without cirrhosis.

Appendices

Appendix A: Abbreviation Key

APRI: AST to platelet ratio
AASLD: American Association for the Study of Liver Diseases
CTP: Child Turcotte Pugh
DAA: direct-acting antiviral
FIB-4: Fibrosis-4 index
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
PAH: pulmonary arterial hypertension
Peg-IFN: pegylated interferon
RBV: ribavirin

Appendix B: 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 (ultrasound-based 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 C: Direct-Acting Antivirals (DAAs) 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			

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

*Combination drugs
**Additional PIs no longer recommended: Victrelis (boceprevir), Incivek (telaprevir)

Appendix D: FDA-Approved Regimens and Treatment Durations

Treatment Naive/Experienced	Genotype	Failed Treatment Regimen	Recommended Regimen *See footnotes for duration*
No Cirrhosis			
Treatment naive	4	None	Technivie§ *If RBV ineligible.*
Not specified	4	Not specified	Technivie + RBV§

§Treatment duration - 12 weeks

Appendix E: AASLD-IDSA Recommended Regimens and Treatment Durations

Treatment Naive/Experienced	Genotype	Failed Treatment Regimen	Recommended Regimen *See footnotes for duration*
No Cirrhosis or Compensated Cirrhosis (CTP/Child-Pugh Class A)			
No prior treatment	4	None	Technivie§
Prior treatment failure	4	Peg-IFN/RBV	Technivie + RBV§

§Treatment duration - 12 weeks

Appendix F: 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.

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
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	10/2016
Added availability of full course of therapy as initial therapy consistent with appendix recommendation for initial criteria Removed continuation criteria	4/17	
Added preferencing information requiring Mavyret for FDA-approved indications. Added requirement for Hep B screening for all patients prior to treatment to ensure that proper risk reduction measures are taken.	9/17	
Annual review. No changes made.	3/18	3/18

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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.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.