



## PRIOR AUTHORIZATION POLICY

**POLICY:** Hepatitis – Technivie™ (ombitasvir/paritaprevir/ritonavir tablets – AbbVie)

**TAC APPROVAL DATE:** 08/23/2017

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### OVERVIEW

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.<sup>1</sup> Technivie combines two direct-acting antivirals (DAAs) with distinct mechanisms of action and non-overlapping resistance profiles to target HCV at multiple steps in the viral lifecycle. Ombitasvir is an inhibitor of HCV NS5A, which is essential for viral RNA replication and virion assembly. Paritaprevir is an inhibitor of HCV NS3/4A protease which is necessary for the proteolytic cleavage of the HCV encoded polyprotein (into mature forms of the NS3, NS4A, NS4B, NS5A, and NS5B proteins) and is essential for viral replication. Ritonavir is not active against HCV. Ritonavir is a potent cytochrome P450 (CYP)3A inhibitor that increases peak and trough plasma drug concentrations of paritaprevir and overall drug exposure (i.e., area under the curve).

### Dosing

The recommended dosage of Technivie is two tablets taken orally once daily (QD) in the morning. Technivie should be taken with a meal but without regard to fat or calorie content. Technivie is used in combination with ribavirin. When administered with Technivie, the recommended dosage of ribavirin is based on weight: 1,000 mg per day for patients < 75 kg and 1,200 mg per day for patients ≥ 75 kg, divided and administered twice-daily (BID) with food. For ribavirin dosage modifications, refer to the ribavirin prescribing information. Monitor liver chemistry tests before initiating and during therapy. The recommended duration of therapy with Technivie + ribavirin in patients with genotype 4 chronic HCV and without cirrhosis is 12 weeks. Technivie administered without ribavirin for 12 weeks may be considered for treatment-naïve patients without cirrhosis who cannot take or tolerate ribavirin.

### Efficacy

The efficacy of Technivie in patients with genotype 4 chronic HCV was established in two clinical trials, one in patients without cirrhosis (PEARL-1) and one in patients with compensated cirrhosis (AGATE-1).<sup>3</sup> See the [Hepatitis C Virus Direct-Acting Antivirals Therapy Class Summary](#) for details.

PEARL-1 was a Phase IIb, multicenter, randomized open-label, in patients with genotype 4 HCV which randomized patients to receive Technivie QD ± weight-based ribavirin (WBR) for 12 weeks. Treatment-experienced patients received Technivie QD + WBR while treatment-naïve patients received Technivie with or without ribavirin. The study did not enroll patients with cirrhosis.

In treatment-naïve patients with genotype 4 chronic HCV, sustained viral response 12 weeks after completion of therapy (SVR12) rates were 100% (n = 42/42) in the WBR-containing arm and 90.9% (n = 40/44) in the non-WBR-containing arm. There was no statistical difference in SVR12 rates between these two treatment groups after adjusting for IL28B genotype (mean difference -9.16%). All treatment-experienced patients in the WBR-containing arm achieved SVR12 (100%, n = 49/49).

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Three treatment-naïve patients who received Technivie without WBR had viral failure: 2% of patients (n = 1/44) had virologic breakthrough at treatment Week 8, and 5% of patients (n = 2/42) relapsed before post-treatment Week 12.

AGATE-1, a Phase III, multi-national, open-label trial randomized adults  $\geq 18$  years of age with genotype 4 chronic HCV with compensated cirrhosis to receive Technivie + WBR for 12 or 16 weeks (n = 120).<sup>7</sup> Eligible patients were treatment-naïve or had previously been treated with pegylated interferon and ribavirin. SVR12 was attained in 97% of patients in the 12 week group and 98% of patients in the 16 week group. In the 12 week group, there was one patient with viral breakthrough.

## Guidelines

The American Association for the Study of Liver Diseases (AASLD) recommended regimens are detailed in the [Hepatitis C Virus Direct-Acting Antivirals Therapy Class Summary](#).<sup>2</sup> For the most up-to-date recommendations always consult the [guidelines](#).

## POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Technivie. All approvals are for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Technivie as well as the monitoring required for adverse events (AEs) and efficacy, approval requires Technivie to be prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or liver transplant physician.

**Automation:** None.

## RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Technivie is recommended in those who meet the following criteria:

### FDA-Approved Indications

- 1. Chronic Hepatitis C Virus (HCV) Genotype 4.** Approve Technivie for 12 weeks if patients meet all of the following criteria (A, B, and C):
  - A)** The patient is  $\geq 18$  years of age; AND
  - B)** Technivie is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician; AND
  - C)** If the patient has compensated cirrhosis (Child-Pugh A), Technivie must be prescribed **in combination with ribavirin**.

Technivie is indicated in combination with ribavirin for the treatment of patients with genotype 4 chronic hepatitis C virus (HCV) infection without cirrhosis and with compensated cirrhosis.<sup>1</sup> Guidelines from the American Association for the Study of Liver Diseases (AASLD) recommend Technivie + weight-based ribavirin (WBR) for treatment-experienced and treatment-naïve patients, including those with cirrhosis. In the AGATE-1 trial, in patients with cirrhosis, Technivie was studied in combination with WBR.<sup>7</sup>

## Other Uses with Supportive Evidence

- 2. Patient Has Been Started on Technivie.** Approve Technivie for an indication or condition addressed as an approval in the Recommended Authorization Criteria section (FDA-Approved Indication). Approve the duration described above to complete a 12-week course therapy (e.g., a patient who should receive 12 weeks, and has received 3 weeks should be approved for 9 weeks to complete their 12-week course).

#### CONDITIONS NOT RECOMMENDED FOR APPROVAL

Technivie has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

- 1. Hepatitis C Virus (HCV), Child-Pugh Class B or Child-Pugh Class C Liver Disease (Moderate or Severe Hepatic Impairment).** Technivie is contraindicated in patients with moderate or severe hepatic impairment (Child-Pugh Class B or C).<sup>1</sup> On October 22, the FDA issued a safety communication about the risk of serious liver injury when Viekira Pak or Technivie are used in patients with moderate or severe hepatic impairment.<sup>5</sup> Hepatic decompensation and liver failure in patients with underlying liver cirrhosis have been reported with the use of Viekira Pak and Technivie. Some of these events have resulted in liver transplant or death. These serious outcomes were reported mostly in patients taking Viekira Pak who had evidence of advanced cirrhosis even before starting treatment. Since the approvals of Viekira Pak in December 2014 and Technivie in July 2015, at least 26 worldwide cases submitted to the FDA Adverse Event Reporting System (FAERS) were considered to be possibly or probably related to Viekira Pak or Technivie. In most of the cases, liver injury occurred within 1 to 4 weeks of starting treatment. Some of the cases occurred in patients for whom these medicines were contraindicated or not recommended. Among these 26 cases, 5 were reported in the US.<sup>6</sup>
- 2. Hepatitis C Virus (HCV) [any genotype], Combination with Any Other DAAs (Not Including Ribavirin).** Technivie provides a complete antiviral regimen for patients with genotype 4 HCV. Technivie is indicated with ribavirin for some patients. In the opinion of a specialist physician reviewing the data we have adopted this criterion.
- 4. Life Expectancy < 12 Months Due to Non-Liver Related Comorbidities.** Patients with limited life expectancy for whom HCV therapy would not improve symptoms or prognosis do not require treatment.<sup>2</sup> According to AASLD guidance, little evidence exists to support initiation of HCV treatment in patients with limited life expectancy (less than 12 months) due to non-liver-related comorbid conditions. For these patients, the benefits of HCV treatment are unlikely to be realized, and palliative care strategies should take precedence.
- 5. Pediatric Patients (Age < 18 Years).** The safety and efficacy of Technivie have not been established in pediatric patients < 18 years of age.<sup>1</sup> In the opinion of a specialist physician reviewing the data we have adopted this criterion.
- 6. Retreatment with Technivie in Patients Who Have Previously Received Viekira Pak/Viekira XR (paritaprevir/ritonavir/ombitasvir + dasabuvir or dasabuvir/ombitasvir/paritaprevir/ritonavir extended-release) or Technivie** (e.g., retreatment in prior null responders, prior partial responders, prior relapse patients, patients who have not completed

a course of therapy due to an adverse reaction or for other reasons). In the opinion of a specialist physician reviewing the data we have adopted this criterion.

- Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

**REFERENCES**

- Technivie™ tablets [prescribing information]. North Chicago, IL: AbbVie, Inc.; March 2017.
- American Association for the Study of Liver Diseases and the Infectious Diseases Society of America. Testing, managing, and treating hepatitis C. Available at: <http://www.hcvguidelines.org>. Updated April 12, 2017. Accessed on: August 14, 2017.
- Hezode C, Asselah T, Reddy KR, et al. Ombitasvir plus paritaprevir plus ritonavir with or without ribavirin in treatment-naïve and treatment-experienced patients with genotype 4 chronic hepatitis C virus infection (PEARL-I): a randomized, open-label trial. *Lancet*. 2015;385(9986):2502-2509.
- Lawitz E, Makara M, Akarca US, et al. Efficacy and safety of ombitasvir, paritaprevir, and ritonavir in an open-label study of patients with genotype 1b chronic hepatitis C virus, with and without cirrhosis. *Gastroenterology*. 2015;149(4):971-978.
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- Asselah T, Hezode C, Qaqish RB, et al. Ombitasvir, paritaprevir, and ritonavir plus ribavirin in adults with hepatitis C virus genotype 4 infection and cirrhosis (AGATE-1): A multicenter, phase 3, randomized open-label trial. *Lancet Gastroenterol Hepatol*. 2016;1(1):25-35..
- Data on file. AbbVie, Inc. March 1, 2017.

**HISTORY**

Type of Revision	Summary of Changes*	TAC Approval Date
New policy	New policy	08/05/2015
Selected revision	Child-Pugh class B or C Liver Disease added to conditions not recommended for approval.	11/11/2015
DEU revision	Updated guidelines	--
Annual revision	No criteria changes. Modified wording in exclusions.	08/10/2016
Selected revision	Concomitant ribavirin requirement added for patients with compensated cirrhosis.	03/08/2017
Annual revision		08/23/2017

TAC – Therapeutic Assessment Committee; \* For a further summary of criteria changes, refer to respective TAC minutes available at: <http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx>; DEU – Drug Evaluation Unit.