Ombitasvir-Paritaprevir-Ritonavir *(Technivie)*

Discontinued. This treatment has been discontinued.

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Drug Summary

Based on data from the PEARL-1 study, the ombitasvir-paritaprevir-ritonavir, given with ribavirin, is an effective all-oral regimen for treatment-naive and treatment-experienced patients with genotype 4 HCV who do not have cirrhosis. At this time, the ombitasvir-paritaprevir-ritonavir regimen should only be used at this time for patients with genotype 4 HCV without cirrhosis; dasabuvir is not included in this regimen since it does not have activity against HCV genotype 4. The effectiveness of ombitasvir-paritaprevir-ritonavir in patients with genotype 4 HCV and cirrhosis is not known. Clinicians need to distinguish the ombitasvir-paritaprevir-ritonavir fixed dose medication (*Technivie*) from the closely related ombitasvir-paritaprevir-ritonavir plus dasabuvir (*Viekira Pak*); the key difference between these two is the absence of medication dasabuvir in the *Technivie* preparation.

Adverse Effects

On October 22, 2015 the United States FDA issued a Drug Safety Warning that treatment with ombitasvir-paritaprevir-ritonavir (*Technive*) can cause serious liver injury, mostly in patients with underlying advanced liver disease. In most of the reported cases, the liver injury occurred within 1 to 4 weeks of starting treatment. In clinical trials, approximately 1% of persons receiving ombitasvir-paritaprevir-ritonavir developed

increases in alanine aminotransferase levels (ALT) to greater than 5 times the upper limit of normal. Because of this potential adverse effect, patients should have hepatic laboratory testing during the first 4 weeks after starting therapy, with further monitoring thereafter as clinically indicated. Among the 135 patients with genotype 4 HCV treated with ombitasvir-paritaprevir-ritonavir, none developed serum ALT levels greater than 5 times the upper limit of normal. The most common adverse effects observed in the PEARL-1 trial for patients receiving ombitasvir-paritaprevir-ritonavir without ribavirin were asthenia (25%), nausea (9%), and fatigue (7%).

Class and Mechanism

Ombitasvir is a NS5A inhibitor with potent pangenotypic picomolar antiviral activity and paritaprevir is an inhibitor of the NS3/4A serine protease. Ritonavir is a potent inhibitor of CYP3A4 enzymes and is used as a pharmacologic booster for paritaprevir—it significantly increases peak and trough paritaprevir plasma concentrations, as well as the area under the curve of paritaprevir. Ritonavir was originally developed and FDA-approved as an HIV protease inhibitor; it does not have activity against HCV.

Manufacturer for United States

Technivie (TEK-ni-vee) is a fixed-dose combination ombitasvir-paritaprevir-ritonavir (Figure 1 and Figure 2). It is manufactured by AbbVie. The closely related combination ombitasvir-paritaprevir-ritonavir plus dasabuvir (*Viekira Pak*) is also manufactured by AbbVie.

FDA Status

On July 24, 2015, the United States Food and Drug Administration (FDA) approved ombitasvir-paritaprevir-ritonavir (*Technivie*), with ribavirin, for the treatment of chronic HCV genotype 4 infection in patients without cirrhosis.

Indications

The fixed-dose combination of ombitasvir-paritaprevir-ritonavir, in combination with ribavirin, is approved for the treatment of patients with chronic HCV genotype 4 infection without cirrhosis. In genotype 4, treatment-naive patients without cirrhosis, ombitasvir-paritaprevir-ritonavir, without ribavirin, may be considered as an option for patients who cannot take or tolerate ribavirin. Ombitasvir-paritaprevir-ritonavir is not recommended for use in patients with moderate hepatic impairment (Child-Pugh B).

Contraindications

Ombitasvir-paritaprevir-ritonavir is contraindicated in following situations:

- Patients with moderate to severe hepatic impairment (Child-Pugh B or C) due to the risk of hepatoxicity.
- With coadministration of drugs that are highly dependent on CYP3A for clearance for which elevated plasma levels could lead to serious toxicity.
- With coadministration of moderate and strong inducers of CYP3A since these medications may lead to reduced efficacy of ombitasvir-paritaprevir-ritonavir.
- In patients who have known hypersensitivity to the medication ritonavir.
- If ribavirin is used in combination with ombitasvir-paritaprevir-ritonavir, the contraindications to ribavirin apply to the treatment regimen.

Dosing

Each tablet of the fixed dose preparation ombitasvir-paritaprevir-ritonavir contains 12.5 mg of ombitasvir, 75 mg of paritaprevir, and 50 mg of ritonavir. The medication is supplied in a monthly carton that has a total of 28 days of therapy. The monthly cartons (Figure 1) contain 4 smaller 1-week supply cartons (Figure 2). The 1-week cartons contain 7 daily dose packs (Figure 3) that each contain two tablets of ombitasvir-paritaprevir-ritonavir.

- Regimen for Treatment of Genotype 4: The recommended dosing for the fixed-dose combination of ombitasvir-paritaprevir-ritonavir is two tablets taken orally once daily in the morning with a meal, but without regard to fat or calorie content. For treatment of genotype 4 infection, ombitasvir-paritaprevir-ritonavir should be administered with ribavirin (weight-based dosing) for a treatment duration of 12 weeks. The weight-based ribavirin dosing is 1000 mg per day in two divided doses for those weighing less than 75 kilograms and 1200 mg per day in two divided doses for patients weighing at least 75 kilograms; ribavirin should be taken with food. For patients with genotype 4 HCV infection who cannot take or tolerate ribavirin, the regimen ombitasvir-paritaprevir-ritonavir without ribavirin for 12 weeks can be considered.
- Renal Impairment: There are no dosage adjustment of ombitasvir-paritaprevir-ritonavir in patients with mild, moderate, or severe renal impairment.
- Hepatic Impairment: For patients with mild hepatic impairment, no dosage adjustment is needed for ombitasvir-paritaprevir-ritonavir. This regimen is not recommended with moderate hepatic impairment (Child-Pugh B) and is contraindicated with severe hepatic impairment (Child-Pugh C).

Clinical Use

The regimen ombitasvir-paritaprevir-ritonavir, with ribavirin, is only indicated for use in patients with genotype 4 HCV. Dasabuvir, which is a component of *Viekira Pak*, does not have activity against genotype 4 HCV and thus is not included in this preparation (*Technivie*).

Cost and Medication Access

The wholesale acquisition cost (WAC) for a 12-week course of ombitasvir-paritaprevir-ritonavir is $76,653,

which corresponds to a cost per day of $912. There are no patient assistance programs listed by AbbVie for ombitasvir-paritaprevir-ritonavir.

Resistance

In the PEARL-1 trial, three treatment-naive patients on ombitasvir-paritaprevir-ritonavir (without ribavirin) developed virologic failure and all three were associated with treatment resistance-associated substitutions, including the the NS3 mutation D168V (with or without Y56H) and the NS5A mutations L28S and L28V (with or without M31I or T58S) in NS5A. All three patients were infected with genotype 4d. Additional *in vitro* mutations have been observed in cell culture.

Key Drug Interactions

For complete information on ombitasvir-paritaprevir-ritonavir-related drug interactions, see the Drug Interactions section in the Ombitasvir-Paritaprevir-Ritonavir (*Technivie*) Prescribing Information.

Full Prescribing Information

Ombitasvir-Paritaprevir-Ritonavir (*Technivie*) Full Prescribing Information

Figures

Figure 1. Daily-Dose Pack

Ombitasvir-Paritaprevir-Ritonavir

Photograph courtesy of AbbVie, Inc.

Figure 2. 1 Week Supply Carton

Ombitasvir-Paritaprevir-Ritonavir

Photograph courtesy of AbbVie, Inc.

Figure 3. Monthly Supply Carton

Ombitasvir-Paritaprevir-Ritonavir

Photograph courtesy of AbbVie, Inc.