PDL DRUG REVIEW

Proprietary Name: Technivie®
Common Name: ombitasvir/paritaprevir/ritonavir
PDL Category: Hepatitis C Agents

Comparable Products	Preferred Drug List Status
Harvoni	Preferred with Conditions

Summary

Indications and Usage: In combination with ribavirin for the treatment of patients with genotype 4 chronic hepatitis C virus (HCV) infection without cirrhosis. Technivie® is not recommended for use in patients with moderate hepatic impairment. This is a pregnancy category B medication. The safety and efficacy of use in children younger than 18 years have not been established.

Dosage Forms: Film-coated Tablets: 12.5mg ombitasvir/75mg paritaprevir/50mg ribavirin

Recommended Dosage: Liver chemistry tests should be monitored prior to and during therapy. Take 2 tablets PO QAM with a meal but without regard to fat or calorie content. Technivie® is used in combination with ribavirin, with the recommended ribavirin dose based on weight (1000mg per day if <75kg and 1200mg per day if ≥75kg, divided and given twice-daily with food). Treatment should be given for 12 weeks.

Technivie® administered without ribavirin for 12 weeks may be considered for treatment-naïve patients who cannot take or tolerate ribavirin.

Dose adjustments are not required for those with renal impairment; however, its use has not been studied in those on dialysis. Dose adjustments are not required for those with mild hepatic impairment. Technivie® is not recommended for use in those with moderate hepatic impairment and use is contraindicated with severe hepatic impairment.

Per the prescribing information: The ritonavir component of Technivie® is also an HIV-1 protease inhibitor and can select for HIV-1 protease inhibitor resistance-associated substitutions. Any HCV/HIV-1 co-infected patients treated with Technivie® should also be on a suppressive antiretroviral drug regimen to reduce the risk of HIV-1 protease inhibitor drug resistance.

Drug Interactions: Concurrent use of Technivie® with the following is not recommended: salmeterol, rilpivirine, lopinavir/ritonavir, atazanavir, atazanavir/ritonavir, voriconazole, and fluticasone. Alternative inhaled or nasal corticosteroids should be considered. Use caution when Technivie® is used with the following: amiodarone, bepridil, disopyramide, flecainide, lidocaine systemic, mexiletine, propafenone, quinidine, furosemide, buprenorphine/naloxone, and alprazolam. Monitor for decreased efficacy of omeprazole and consider increasing the omeprazole dose (avoid use of ≥40mg omeprazole/day). Dose adjustments may be required with some drug

combinations with Technivie®. It is recommended to monitor digoxin levels and decrease the digoxin dose by 30-50%. The max daily dose of ketoconazole should be limited to 200mg/day. It is recommended to consider reducing the dose of amlodipine. It is recommended to use darunavir 800mg (without ritonavir) if used with Technivie®. The dose of pravastatin should not exceed 40mg daily. The dose of cyclosporine and tacrolimus should be reduced. Last, it is recommended to consider alternative anti-HCV therapy in patients taking quetiapine. Also, refer to drugs that are contraindicated with Technivie®.

Common Adverse Drug Reactions: *There was no placebo data, thus the* ***l****isted % incidence for adverse drug reactions= reported % incidence for drug (ombitasvir, paritaprevir, ritonavir plus ribavirin).* The most frequently reported adverse events included asthenia (29%), fatigue (15%), nausea (14%), insomnia (13%), pruritus (7%), and skin reactions (7%). The mean change from baseline in hemoglobin levels was -2.1g/dl. In addition, post-baseline elevations in bilirubin ≥2 times the upper limit of normal (ULN) was seen in 5% of treated subjects.

Contraindications: The contraindications to ribavirin also apply to this combination regimen. Refer to the ribavirin prescribing information for a list of contraindications to ribavirin. Technivie® is contraindicated: in patients with severe hepatic impairment; with drugs that are highly dependent on CYP3A for clearance and for which elevated plasma levels are associated with serious and/or life-threatening events; with drugs that are moderate or strong inducers of CYP3A; in patients with known hypersensitivity to ritonavir. Specific drugs contraindicated with Technivie® include: alfuzosin, carbamazepine, phenytoin, phenobarbital, rifampin, ergotamine, dihydroergotamine, ergonovine, methylergonovine, ethinyl estradiol containing meds (such as combined oral contraceptives), St. Johns' wort, lovastatin, simvastatin, pimozide, efavirenz, sildenafil when dosed as Revatio® for PAH, triazolam, and oral midazolam.

Manufacturer: AbbVie

Analysis: Technivie® is a fixed-dose combination tablet containing ombitasvir (a HCV NS5A inhibitor), paritaprevir (a HCV NS3/4A protease inhibitor), and ritonavir (a CYP3A inhibitor that provides increased plasma levels of paritaprevir). Both ombitasvir and paritaprevir are considered direct-acting HCV antiviral agents, but with their own distinct mechanism of action. Ritonavir is not active against HCV.

The safety and efficacy of Technivie® was established in one multicenter, open-label, randomized study (PEARL-1) that included subjects with HCV infection genotype 4 without cirrhosis (N=135) who were either treatment-naïve or did not achieve a virologic response with prior treatment with pegylated interferon/ribavirin. Previous exposure to HCV direct-acting antivirals was prohibited. The primary endpoint was sustained virologic response (SVR) 12 weeks after the end of treatment (SVR12), and results are illustrated in the table below. (Note that in table below, 'other' includes subjects not achieving SVR12 but not experiencing on-treatment virologic failure or relapse.)

	ombitasvir/paritaprevir/ritonavir with ribavirin		ombitasvir/paritaprevir/ritonavir
Treatment Outcomes	Treatment-Naïve (N=42)	Treatment-Experienced (N=49)	Treatment-naïve (N=44)
Overall SVR	100%	100%	91%
Outcomes for subjects without SVR			
On-treatment virologic failure	0%	0%	2%
Relapse	0%	0%	5%
Other	0%	0%	2%

Of the 131 patients in PEARL-1 who achieved SVR12, virologic response data at post-treatment week 24 were available for 129 patients; 100% of these subjects maintained response through 24 weeks post-treatment (SVR24).

Place in Therapy: Technivie® is the first product FDA approved for the treatment of genotype 4 HCV infection to be used without the need for concomitant use with interferon. Significant drug interactions need to be monitored, as this product contains ritonavir, a potent CYP3A inhibitor. In addition, liver enzymes need to be monitored, as use is not recommended in moderate hepatic impairment and is contraindicated in severe hepatic impairment. The evidence-based IDSA/AASLD guidelines are frequently updated and include several recommended regimens for genotype 4 infections, one of which is Technivie®. Hepatitis C treatment is a rapidly changing therapeutic area and the recommendation for treatment for specific genotypes and clinical situations are continuing to evolve.

Technivie® should be added to the PDL as preferred and require clinical prior authorization to verify diagnosis, assessment of liver function, and to monitor for drug interactions.

PDL Placement: ☒ **Preferred with Conditions**
☐ **Non-Preferred**

References

[1] Technivie [package insert]. North Chicago, IL: AbbVie Inc; 2015.

[2] FDA News Release: FDA approves Technivie for treatment of chronic hepatitis C genotype 4. Website: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm455857.htm. Accessed August 2015.

[3] American Association for the Study of Liver Diseases and the Infectious Diseases Society of America. (2015) Recommendations for Testing, Managing, and Treating Hepatitis C. Available at http://www.hcvguidelines.org/sites/default/files/full_report.pdf Accessed August 2015.