RATIONALE FOR INCLUSION IN PA PROGRAM

Background
Hepatitis C is a viral disease that causes inflammation of the liver that can lead to diminished liver function or liver failure. Most people infected with hepatitis C virus (HCV) have no symptoms of the disease until liver damage becomes apparent, which may take several years. Some people with chronic HCV infection develop scarring and poor liver function (cirrhosis) over many years, which can lead to complications such as bleeding, jaundice (yellowish eyes or skin), fluid accumulation in the abdomen, infections or liver cancer (1).

Technivie (ombitasvir, paritaprevir and ritonavir) is used in combination with ribavirin for the treatment of hepatitis C virus (HCV) genotype 4 infections in patients without scarring or poor liver function (cirrhosis) (1).

Regulatory Status
FDA-approved indications: Technivie is a fixed-dose combination of ombitasvir, a hepatitis C virus NS5A inhibitor, paritaprevir, a hepatitis C virus NS3/4A protease inhibitor, and ritonavir, a CYP3A inhibitor and is indicated in combination with ribavirin for the treatment of patients with genotype 4 chronic hepatitis C virus (HCV) infection without cirrhosis (2).

No dosage adjustment of Technivie is required in patients with mild hepatic impairment (Child-Pugh A). Technivie is contraindicated in patients with severe hepatic impairment (Child-Pugh C) due to potential toxicity (2).

Hepatic decompensation and hepatic failure, including liver transplantation, have been reported postmarketing in patients treated with Technivie. Most patients with these severe outcomes had evidence of advanced cirrhosis prior to initiating therapy. Reported cases typically occurred within one to four weeks of initiating therapy and were characterized by the acute onset of rising direct serum bilirubin levels without ALT elevations in association with clinical signs and symptoms of hepatic decompensation (3).

If Technivie is administered with ribavirin, the contraindications to ribavirin also apply to this combination regimen. The primary toxicity of ribavirin is hemolytic anemia. The boxed warning explains that the anemia associated with ribavirin therapy may result in worsening of cardiac disease that has led to fatal and nonfatal myocardial infarctions. Patients with a history of
significant or unstable cardiac disease should not be treated with ribavirin (3).

There is a boxed warning stating that ribavirin may cause birth defects and fetal death. Significant teratogenic and embryocidal effects have been demonstrated in all animal species exposed to ribavirin. In addition, ribavirin has a multiple-dose half-life of 12 days, and so it may persist in nonplasma compartments for as long as 6 months. Therefore, ribavirin therapy is contraindicated in women who are pregnant and in the male partners of women who are pregnant. Extreme care must be taken to avoid pregnancy during therapy and for 6 months after completion of treatment in both female patients and in female partners of male patients who are taking ribavirin therapy. At least two reliable forms of effective contraception must be utilized during treatment and during the 6-month post-treatment follow-up period (3).

Hepatic laboratory testing on all patients during the first 4 weeks of treatment must be performed because elevations of alanine transaminase (ALT) to greater than 5 times the upper limit of normal (ULN) may occur with Technivie with or without ribavirin. ALT elevations were significantly more frequent in female subjects who were using ethinyl estradiol-containing medications such as combined oral contraceptives, contraceptive patches or contraceptive vaginal rings. Ethinyl estradiol-containing medications must be discontinued prior to starting therapy with Technivie. Alternative methods of contraception (e.g., progestin only contraception or non-hormonal methods) are recommended during Technivie therapy. Ethinyl estradiol-containing medications can be restarted approximately 2 weeks following completion of treatment with Technivie (2).

Cross-resistance may occur among NS5A inhibitors and among NS3/4A protease inhibitors within each individual class. The impact of prior ombitasvir or paritaprevir treatment experience on the efficacy of other NS5A inhibitors or NS3/4A protease inhibitors has not been studied. Similarly, the efficacy of Technivie has not been studied in subjects who have failed prior treatment with another NS5A inhibitor, NS3/4A protease inhibitor, or NS5B inhibitor (2).

Safety and effectiveness of Technivie in children less than 18 years of age have not been established (2).

**Summary**

Hepatitis C is a viral disease that causes inflammation of the liver that can lead to diminished liver function or liver failure (1). Technivie contains two new drugs - ombitasvir, and paritaprevir that work together to inhibit the growth of HCV. Technivie also contains ritonavir which is used to
increase blood levels of paritaprevir. Technivie can be used with or without ribavirin, but it is not recommended for patients whose liver is unable to function properly (decompensated cirrhosis). Safety and effectiveness of Technivie in children less than 18 years of age have not been established (2).

Prior authorization is required to ensure the safe, clinically appropriate and cost effective use of Technivie while maintaining optimal therapeutic outcomes.

References