

U.S. FDA Grants Priority Review to AbbVie for Investigational, All-Oral, Interferon-Free Therapy for the Treatment of Genotype 4 Chronic Hepatitis C

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NORTH CHICAGO, Ill., April 24, 2015 /PRNewswire/ -- AbbVie (NYSE: ABBV) has announced that the U.S. Food and Drug Administration (FDA) has accepted its New Drug Application (NDA) and granted priority review for the company's, all-oral, interferon-free, two direct-acting antiviral treatment of ombitasvir, paritaprevir, ritonavir (OBV/PTV/r), with ribavirin (RBV). The NDA is for the treatment of adults with chronic genotype 4 (GT4) hepatitis C virus (HCV) infection.

AbbVie's regimen is the first all-oral, interferon-free therapy being evaluated by the FDA for patients in the United States with chronic GT4 HCV infection. This submission affirms the company's commitment to seeking access to curative* therapy for patients living with chronic HCV infection (*curative is defined as when the virus is no longer detectable in the patient's blood 12 weeks after treatment ends; sustained virologic response [SVR12]).

The FDA granted priority review to AbbVie for the regimen based in part on data from the PEARL-I study, which was recently published online in *The Lancet*. The FDA grants priority review designation to investigational therapies that treat a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. This designation shortens the regulatory review period for non-new chemical entity NDAs from the normal 10 months to six months.

AbbVie's regimen was also granted a Breakthrough Therapy designation by the FDA on June 30, 2014, a status given to investigational treatments for serious or life-threatening conditions with preliminary clinical evidence that may demonstrate substantial improvement on at least one clinically significant endpoint compared to available therapy.¹

"We are pleased that the FDA has granted priority review for our all-oral, interferon-free treatment for patients with chronic GT4 HCV infection," said Michael Severino, M.D., executive vice president, research and development and chief scientific officer, AbbVie. "Submission of this NDA further underscores AbbVie's commitment to developing therapies to treat a wide range of patients living with chronic HCV infection."

PEARL-I is an open-label, Phase 2b study that demonstrated 100 percent of GT4 patients without cirrhosis who were new to therapy (n=42/42) or who had failed previous treatment with pegylated interferon (pegIFN) and RBV (n=49/49) achieved SVR12 after receiving OBV/PTV/r and RBV for 12 weeks. Additionally, 91 percent of patients who were new to therapy achieved SVR12 (n=40/44) after taking the treatment without RBV.

The Centers for Disease Control and Prevention (CDC) estimates that in the United States, 3.2 million people are chronically infected with HCV.² While genotype 1 (GT1) is the most prevalent form of HCV in the U.S., accounting for approximately 73 percent of all cases, GT4 infection accounts for up to 6 percent of HCV infections.^{3,4} Hepatitis C is inflammation of the liver caused by an infection with HCV.⁵ It is transmitted when an infected person's blood enters the bloodstream of another person.⁶ There are six major HCV genotypes (GT1-6).⁷ Presently, there is no vaccine for HCV infection.²

About the PEARL-I Study

PEARL-I is an open-label, Phase 2b study designed to evaluate the safety and efficacy of 12 weeks of treatment with OBV/PTV/r with and without RBV in non-cirrhotic adult patients with chronic GT4 HCV infection who were new to therapy or had failed previous treatment with pegylated interferon and RBV.

Treatment-naïve GT4 patients were randomized in a 1:1 ratio to receive OBV/PTV/r with or without RBV. All treatment-experienced GT4 patients received OBV/PTV/r with RBV. In the treatment-naïve group without RBV, on-treatment virologic breakthrough was reported in one patient (2 percent) and two patients (5 percent) experienced post-treatment relapse. There were no virologic failures in the other treatment arms. Patients with GT1b HCV infection were also studied but not included in the efficacy analysis for the NDA submission; the results in patients with GT4 HCV were reported in *The Lancet*.

There were no discontinuations due to adverse events in PEARL-I. The most commonly reported treatment-emergent adverse events (greater than 15 percent in any group) were headache (29-33 percent), asthenia (weakness) (24-33 percent), fatigue (7-18 percent), nausea (9-17 percent) and insomnia (5-16 percent). One patient had a grade 3 liver function test elevation (aspartate aminotransferase [AST] greater than five times the upper limit of normal), which was asymptomatic and resolved during continued dosing. Four patients with hemoglobin decreases (anemia) required RBV dose reductions; however, none of these patients required blood transfusions or medication to boost their red blood cell production.

About AbbVie's Two Direct-Acting Antiviral HCV Treatment

AbbVie's proposed all-oral antiviral treatment consists of the fixed-dose combination of paritaprevir/ritonavir (150/100mg) co-formulated with ombitasvir (25mg) dosed once daily, co-administered with weight-based ribavirin (1000mg or 1200mg in divided doses, twice daily). The combination of two direct-acting antivirals, each with distinct mechanisms of action, targets and inhibits specific HCV proteins in the viral replication process.

About AbbVie's HCV Clinical Development Program

AbbVie's HCV clinical development program is intended to advance scientific knowledge and clinical care by investigating interferon-free, all-oral treatments with and without ribavirin with the goal of achieving high sustained virologic response rates in as many patients as possible. AbbVie's development programs combining two direct-acting antivirals are studying additional hepatitis C virus (HCV) genotypes.

Paritaprevir was discovered during the ongoing collaboration between AbbVie and Enanta Pharmaceuticals (NASDAQ: ENTA) for HCV protease inhibitors and regimens that include protease inhibitors. Paritaprevir is being developed by AbbVie for use in combination with AbbVie's other investigational medicines for the treatment of hepatitis C.

Safety Information

Ombitasvir, paritaprevir, and ritonavir (OBV/PTV/r) and RBV are not approved for the investigational use discussed above, and no conclusions can or should be drawn regarding the safety or efficacy of these products for this use. There are special safety considerations when prescribing these drugs in approved populations.

OBV/PTV/r must not be used in patients with severe hepatic impairment or with certain medications, which may result in serious and/or life-threatening events or loss of therapeutic effect. OBV/PTV/r can cause increases in certain liver enzyme levels (ALT) and should be monitored during the first four weeks of treatment, and then as clinically indicated thereafter. Female patients should not take ethinyl estradiol-containing medications during treatment with OBV/PTV/r, as they are at greater risk for liver enzyme elevations when taking these medications.

Ritonavir must also not be used in patients with known hypersensitivity to ritonavir or any of its excipients.

Ribavirin monotherapy is not effective for the treatment of chronic hepatitis C virus and must not be used alone for this use. Ribavirin causes significant teratogenic effects and must not be used in women who are pregnant or breast-feeding and in men whose female partners are pregnant. Ribavirin must not be used in patients with a history of severe pre-existing cardiac disease, severe hepatic dysfunction or decompensated cirrhosis of the liver, autoimmune hepatitis, hemoglobinopathies, or in combination with peginterferon alfa-2a in HIV/HCV co-infected patients with cirrhosis and Child-Pugh score ≥ 6 . See approved product labels for more information.