Bayer HealthCare

Intended for U.S. media only

News Release

FDA Approves Bayer's New Class of Drug Adempas® (riociguat) tablets to Treat Adults with PAH and Persistent, Recurrent or Inoperable CTEPH

First and only drug approved in U.S. to Treat Two Forms of Pulmonary Hypertension (WHO Group 1 and 4)

WHIPPANY, N.J., October 8, 2013 – Bayer HealthCare announced today that the United States Food and Drug Administration (FDA) has approved Adempas® (riociguat) tablets for: (i) the treatment of adults with persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH) (WHO* Group 4) after surgical treatment or inoperable CTEPH to improve exercise capacity and WHO functional class; and (ii) the treatment of adults with pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise capacity, improve WHO functional class and delay clinical worsening.

In PAH, efficacy was shown in patients on Adempas monotherapy or in combination with endothelin receptor antagonists (ERAs) or prostanoids (inhaled, oral or subcutaneous). Studies establishing effectiveness included predominately patients with WHO functional class II-III and etiologies of idiopathic or heritable PAH (61%) or PAH associated with connective tissue diseases (25%).

Adempas is the only treatment approved in the U.S. for use in two types of pulmonary hypertension (WHO Group 1 and 4). It is the first and only FDA-approved drug therapy for persistent/recurrent CTEPH after surgical treatment or inoperable CTEPH. It is also the only approved oral therapy in PAH with efficacy shown in monotherapy or in combination with ERAs or prostanoids.

For all female patients, Adempas is available only through a restricted program called the Adempas Risk Evaluation and Mitigation Strategy (REMS) Program.

---

* World Health Organization

“CTEPH and PAH are serious and life-threatening diseases,” said Nick H. Kim, Associate Clinical Professor of Medicine, Division of Pulmonary and Critical Care Medicine; Director, Pulmonary Vascular Medicine; Director, Fellowship Program; University of California San Diego. “The approval of Adempas equips physicians with a new approach to treating PAH patients, and it gives us the first approved drug treatment for patients with inoperable CTEPH or with persistent/recurrent CTEPH after surgery. While surgery should always be considered as the first treatment option for CTEPH, the fact remains that up to forty percent of CTEPH patients are not eligible for surgery, and ten to thirty-five percent of CTEPH patients have disease that persists after surgery.”

PAH is a disease characterized by elevated pressure in the pulmonary arteries. CTEPH is a form of pulmonary hypertension in which blood clots and thromboembolic occlusion of the pulmonary vessels leads to increased pressure in the pulmonary arteries. The standard treatment for CTEPH is pulmonary endarterectomy, a potentially curative surgery that clears clots and scar material from the blood vessels of the lung.

“Bayer is deeply committed to bringing new treatment options to patients with life-threatening diseases. Adempas is an excellent example of this commitment, because it is the result of years of dedicated research in our Bayer laboratories into a new way of treating two forms of pulmonary hypertension,” said Pamela A. Cyrus, MD, Vice President and Head, U.S. Medical, Bayer HealthCare Pharmaceuticals. “We are pleased to bring this new class of treatment to patients with PAH or with inoperable CTEPH or persistent/recurrent CTEPH after surgical treatment.”

Rino Aldrighetti, President and CEO, Pulmonary Hypertension Association added, “From a patient's perspective, living with pulmonary hypertension remains difficult. We know that not all treatments work for all people. We get excited when there is a new treatment option for PAH patients, and we are thrilled there is finally an approved drug treatment for people living with persistent/recurrent CTEPH after surgical treatment or inoperable CTEPH.”

Adempas, a stimulator of soluable guanylate cyclase (sGC), represents a new class of drug now available in the U.S. Pulmonary hypertension is associated with endothelial dysfunction, impaired synthesis of nitric oxide (NO) and insufficient stimulation of the NO-sGC-cGMP pathway. Adempas sensitizes sGC to endogenous NO by stabilizing the NO-sGC binding. Adempas also directly stimulates sGC via a different binding site independently of NO. Adempas restores the NO-sGC-cGMP pathway and leads to increased generation of cGMP with subsequent vasodialation.

The most common adverse reactions occurring more frequently ($\geq$3%) on Adempas than placebo were headache (27% vs 18%), dyspepsia/gastritis (21% vs. 8%), dizziness (20% vs. 13%), nausea (14% vs.

11%), diarrhea (12% vs. 8%), hypotension (10% vs. 4%), vomiting (10% vs. 7%), anemia (7% vs. 2%), gastroesophageal reflux disease (5% vs. 2%), and constipation (5% vs. 1%). Other events that were seen more frequently in Adempas compared to placebo and potentially related to treatment were: palpitations, nasal congestion, epistaxis, dysphagia, abdominal distension and peripheral edema.

About Patient Assistance Program

Bayer offers patient assistance through the Adempas Aim Support Center program, which will assist with obtaining coverage and patient support of Adempas. Patients and providers may contact the program at 1-855-4ADEMPAS for additional information.

IMPORTANT SAFETY INFORMATION

WARNING: EMBRYO-FETAL TOXICITY

Do not administer Adempas (riociguat) tablets to a pregnant female because it may cause fetal harm.

Females of reproductive potential: Exclude pregnancy before the start of treatment, monthly during treatment, and 1 month after stopping treatment. Prevent pregnancy during treatment and for one month after stopping treatment by using acceptable methods of contraception.

For all female patients, Adempas is available only through a restricted program called the Adempas Risk Evaluation and Mitigation Strategy (REMS) Program.

Contraindications

Adempas is contraindicated in:

- Pregnancy. Adempas may cause fetal harm when administered to a pregnant woman. Adempas was consistently shown to have teratogenic effects when administered to animals. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus.
- Co-administration with nitrates or nitric oxide donors (such as amyl nitrite) in any form.
- Concomitant administration with phosphodiesterase (PDE) inhibitors, including specific PDE-5 inhibitors (such as sildenafil, tadalafil, or vardenafil) or nonspecific PDE inhibitors (such as dipyridamole or theophylline).

Warnings and Precautions

Embryo-Fetal Toxicity. Adempas may cause fetal harm when administered during pregnancy and is contraindicated for use in women who are pregnant. In females of reproductive potential, exclude pregnancy prior to initiation of therapy, advise use of acceptable contraception and obtain monthly pregnancy tests. For females, Adempas is only available through a restricted program under the Adempas REMS Program.

Adempas REMS Program. Females can only receive Adempas through the Adempas REMS Program, a restricted distribution program.

Important requirements of the Adempas REMS program include the following:

- Prescribers must be certified with the program by enrolling and completing training.
- All females, regardless of reproductive potential, must enroll in the Adempas REMS Program prior to initiating Adempas. Male patients are not enrolled in the Adempas REMS Program.
- Female patients of reproductive potential must comply with the pregnancy testing and contraception requirements.
- Pharmacies must be certified with the program and must only dispense to patients who are authorized to receive Adempas.

Further information, including a list of certified pharmacies, is available at www.AdempasREMS.com or 1-855-4ADEMPAS.

Hypotension. Adempas reduces blood pressure. Consider the potential for symptomatic hypotension or ischemia in patients with hypovolemia, severe left ventricular outflow obstruction, resting hypotension, autonomic dysfunction, or concomitant treatment with antihypertensives or strong CYP and P-gp/BCRP inhibitors. Consider a dose reduction if patient develops signs or symptoms of hypotension.

Bleeding. In the placebo-controlled clinical trials program, serious bleeding occurred in 2.4% of patients taking Adempas compared to 0% of placebo patients. Serious hemoptysis occurred in 5 (1%) patients taking Adempas compared to 0 placebo patients, including one event with fatal outcome. Serious hemorrhagic events also included 2 patients with vaginal hemorrhage, 2 with catheter site hemorrhage, and 1 each with subdural hematoma, hematemesis, and intra-abdominal hemorrhage.

Pulmonary Veno-Occlusive Disease. Pulmonary vasodilators may significantly worsen the cardiovascular status of patients with pulmonary veno-occlusive disease (PVOD). Therefore, administration of Adempas to such patients is not recommended. Should signs of pulmonary edema occur, the possibility of associated PVOD should be considered and if confirmed, discontinue treatment with Adempas.

Most Common Adverse Reactions

The most common adverse reactions occurring more frequently (≥3%) on Adempas than placebo were headache (27% vs. 18%), dyspepsia/gastritis (21% vs. 8%), dizziness (20% vs. 13%), nausea (14% vs. 11%), diarrhea (12% vs. 8%), hypotension (10% vs. 4%), vomiting (10% vs. 7%), anemia (7% vs. 2%), gastroesophageal reflux disease (5% vs. 2%), and constipation (5% vs. 1%).

Other events that were seen more frequently in Adempas compared to placebo and potentially related to treatment were: palpitations, nasal congestion, epistaxis, dysphagia, abdominal distension and peripheral edema.

For important risk and use information, please see the full Prescribing Information, including Boxed Warning, at www.adempas-us.com.

About Bayer HealthCare Pharmaceuticals Inc.

Bayer HealthCare Pharmaceuticals Inc. is the U.S.-based pharmaceuticals business of Bayer HealthCare LLC, a subsidiary of Bayer AG. Bayer HealthCare is one of the world's leading, innovative companies in the healthcare and medical products industry, and combines the activities of the

Animal Health, Consumer Care, Medical Care, and Pharmaceuticals divisions. As a specialty pharmaceutical company, Bayer HealthCare provides products for General Medicine, Hematology, Neurology, Oncology and Women's Healthcare. The company's aim is to discover and manufacture products that will improve human health worldwide by diagnosing, preventing and treating diseases.

###

Intended for U.S. media only

Media Contact:
Marcy Funk, Communications, Bayer HealthCare
Telephone: (862) 404-5385
E-Mail: marcy.funk@bayer.com

Forward-Looking Statements

This release may contain forward-looking statements based on current assumptions and forecasts made by Bayer Group or subgroup management. Various known and unknown risks, uncertainties and other factors could lead to material differences between the actual future results, financial situation, development or performance of the company and the estimates given here. These factors include those discussed in Bayer's public reports which are available on the Bayer website at www.bayer.com. The company assumes no liability whatsoever to update these forward-looking statements or to conform them to future events or developments.