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U.S. Food and Drug Administration accepts filing of new drug application for empagliflozin/metformin fixed-dose combination

RIDGEFIELD, Conn. and INDIANAPOLIS, Oct. 21, 2014 /PRNewswire/ -- The U.S. Food and Drug Administration (FDA) has accepted the filing of a New Drug Application (NDA) for empagliflozin plus immediate-release metformin hydrochloride fixed-dose combination, an investigational compound being studied for the treatment of adults with type 2 diabetes (T2D). Empagliflozin plus metformin is part of the Boehringer Ingelheim and Eli Lilly and Company (NYSE: LLY) Diabetes alliance portfolio.

"Type 2 diabetes is a progressive condition, and many patients eventually require multiple medications to manage their blood sugar," said Christophe Arbet-Engels, M.D., Ph.D., vice president, metabolic-clinical development and medical affairs, Boehringer Ingelheim Pharmaceuticals, Inc. "The FDA's acceptance of the NDA for the empagliflozin plus metformin fixed-dose combination brings us one step closer to offering a potential new treatment option that may help patients better manage their type 2 diabetes through one pill that combines two distinct approaches to help control blood sugar."

Empagliflozin is a sodium glucose co-transporter-2 (SGLT2) inhibitor, which removes excess glucose through the urine by blocking glucose reabsorption in the kidney. Metformin, a commonly prescribed initial treatment for T2D, decreases the production of glucose in the liver and its absorption in the intestine and improves the body's ability to utilize glucose.

The filing includes data from multiple clinical trials examining the co-administration of empagliflozin and metformin in the treatment of 4,740 adults with T2D.

Empagliflozin, marketed as Jardiance® (empagliflozin) tablets in the U.S., was approved by the FDA in August 2014 as an adjunct to diet and exercise to improve glycemic control in adults with T2D. JARDIANCE is not recommended for people with type 1 diabetes or for the treatment of diabetic ketoacidosis (increased ketones in the blood or urine).

About Diabetes

Approximately 29 million Americans and an estimated 382 million people worldwide have type 1 or type 2 diabetes, and nearly 28 percent of Americans with diabetes—totaling 8 million people—are undiagnosed. In the U.S., approximately 12 percent of those aged 20 and older have diabetes. T2D is the most common type, accounting for an estimated 90 to 95 percent of all adult diabetes cases in the U.S. Diabetes is a chronic condition that occurs when the body either does not properly produce, or use, the hormone insulin.

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about JARDIANCE?

JARDIANCE can cause serious side effects, including:

- **Dehydration.** JARDIANCE can cause some people to have dehydration (the loss of body water and salt). Dehydration may cause you to feel dizzy, faint, light-headed, or weak, especially when you stand up.

You may be at a higher risk of dehydration if you:

- have low blood pressure
 - take medicines to lower your blood pressure, including water pills (diuretics)
 - are on a low salt diet
 - have kidney problems
 - are 65 years of age or older.
- **Vaginal yeast infection.** Women who take JARDIANCE may get vaginal yeast infections. Talk to your doctor if you experience vaginal odor, white or yellowish vaginal discharge (discharge may be lumpy or look like cottage cheese), and/or vaginal itching.

- **Yeast infection of the penis.** Men who take JARDIANCE may get a yeast infection of the skin around the penis, especially uncircumcised males and those with chronic infections. Talk to your doctor if you experience redness, itching or swelling of the penis, rash of the penis, foul smelling discharge from the penis, and/or pain in the skin around penis.

Who should not take JARDIANCE?

- **Do not take JARDIANCE** if you are allergic to empagliflozin or any of the ingredients in JARDIANCE.

Symptoms of serious allergic reactions to JARDIANCE may include:

- skin rash
- raised red patches on your skin (hives)
- swelling of the face, lips, tongue, and throat that may cause difficulty breathing or swallowing.

If you have any of these symptoms, stop taking JARDIANCE and contact your doctor or go to the nearest emergency room right away.

- **Do not take JARDIANCE** if you have severe kidney problems or are on dialysis.

What should I tell my doctor before using JARDIANCE?

Tell your doctor if you:

- have kidney problems. Your doctor may do blood tests to check your kidneys before and during your treatment with JARDIANCE
- have liver problems
- have a history of urinary tract infections or problems with urination
- have any other medical conditions
- are pregnant or planning to become pregnant. It is unknown if JARDIANCE will harm your unborn baby
- are breastfeeding, or plan to breastfeed. It is unknown if JARDIANCE passes into your breast milk.

Tell your doctor about all the medicines you take including prescription and over-the-counter medicines, vitamins, and herbal supplements. Especially tell your doctor if you take water pills (diuretics) or medicines that can lower your blood sugar such as insulin.

What are other possible side effects of JARDIANCE?

- **Low blood sugar** (hypoglycemia): if you take JARDIANCE with another medicine that can cause low blood sugar, such as sulfonylurea or insulin, your risk of low blood sugar is higher. The dose of your sulfonylurea or insulin may need to be lowered. Symptoms of low blood sugar may include:
 - Headache
 - Drowsiness
 - Weakness
 - Dizziness
 - Confusion
 - Irritability
 - Hunger
 - Fast heart beat
 - Sweating
 - Shaking or feeling jittery
- **Kidney Problems**, especially in people 75 years of age or older and people who already have kidney problems
- **Urinary Tract Infection**: symptoms may include burning feeling when passing urine, pain in the pelvis or back, or urine that looks cloudy
- **Increased fats in your blood (cholesterol).**

The most common side effects of JARDIANCE include urinary tract infections, and yeast infections in females.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

For more information, please see full [Prescribing Information, including Patient Information](#).

Boehringer Ingelheim and Eli Lilly and Company

In January 2011, Boehringer Ingelheim and Eli Lilly and Company announced an alliance in diabetes that centers on compounds representing several of the largest diabetes treatment classes. The alliance leverages the strengths of two of the world's leading pharmaceutical companies. By joining forces, the companies demonstrate commitment in the care of people with diabetes and stand together to focus on patient needs. Find out more about the alliance at www.boehringer-ingelheim.com or www.lilly.com.

About the Boehringer Ingelheim Cares Foundation Patient Assistance Programs

For more than 125 years, Boehringer Ingelheim has been focused on improving the lives of patients. In keeping with the company commitment to do the most good for the most people, Boehringer Ingelheim works hard to ensure its medicines are accessible to everyone who needs them, including senior citizens and families on limited incomes. The Boehringer Ingelheim Cares Foundation Patient Assistance Programs (BI-PAP) make Boehringer Ingelheim medicines available free of charge to patients who are without pharmaceutical insurance coverage, and who meet certain household income levels.

About Boehringer Ingelheim Pharmaceuticals, Inc.

Boehringer Ingelheim Pharmaceuticals, Inc., based in Ridgefield, CT, is the largest U.S. subsidiary of Boehringer Ingelheim Corporation (Ridgefield, CT) and a member of the Boehringer Ingelheim group of companies.

The Boehringer Ingelheim group is one of the world's 20 leading pharmaceutical companies. Headquartered in Ingelheim, Germany, it operates globally with 142 affiliates and more than 47,400 employees. Since it was founded in 1885, the family-owned company has been committed to researching, developing, manufacturing and marketing novel medications of high therapeutic value for human and veterinary medicine.

Social responsibility is a central element of Boehringer Ingelheim's culture. Involvement in social projects, caring for employees and their families, and providing equal opportunities for all employees form the foundation of the global operations. Mutual cooperation and respect, as well as environmental protection and sustainability are intrinsic factors in all of Boehringer Ingelheim's endeavors.

In 2013, Boehringer Ingelheim achieved net sales of about \$18.7 billion (14.1 billion euro). R&D expenditure in the Prescription Medicines business corresponds to 19.5% of its net sales.

For more information please visit <http://www.us.boehringer-ingelheim.com>.

About Lilly Diabetes

Lilly has been a global leader in diabetes care since 1923, when we introduced the world's first commercial insulin. Today we are building upon this heritage by working to meet the diverse needs of people with diabetes and those who care for them. Through research and collaboration, a broad and growing product portfolio and a continued determination to provide real solutions—from medicines to support programs and more—we strive to make life better for all those affected by diabetes around the world. For more information, visit www.lillydiabetes.com.

About Eli Lilly and Company

Lilly is a global healthcare leader that unites caring with discovery to make life better for people around the world. We were founded more than a century ago by a man committed to creating high-quality medicines that meet real needs, and today we remain true to that mission in all our work. Across the globe, Lilly employees work to discover and bring life-changing medicines to those who need them, improve the understanding and management of disease, and give back to communities through philanthropy and volunteerism. To learn more about Lilly, please visit us at www.lilly.com, @LillyHealth on Twitter and <http://newsroom.lilly.com/social-channels>.

This press release contains forward-looking statements about an empagliflozin and metformin fixed-dose combination for the treatment of type 2 diabetes. It reflects Lilly's current beliefs; however, as with any such undertaking, there are substantial risks and uncertainties in the process of drug development and commercialization. There is no guarantee that future study results and patient experience will be consistent with study findings to date or that an empagliflozin and metformin combination tablet will prove to be commercially successful. For further discussion of these and other risks and uncertainties, please see Lilly's latest Forms 10-Q and 10-K filed with the U.S. Securities and Exchange Commission. Lilly undertakes no duty to update forward-looking statements.

Jardiance® is a registered trademark of Boehringer Ingelheim.

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To view the original version on PR Newswire, visit: <http://www.prnewswire.com/news-releases/us-food-and-drug-administration-accepts-filing-of-new-drug-application-for-empagliflozinmetformin-fixed-dose-combination-512026316.html>

SOURCE Eli Lilly and Company; Boehringer Ingelheim

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