



Boehringer Ingelheim and Lilly expand heart failure program for Jardiance® with new exercise capacity trials

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EMPERIAL clinical trials will evaluate the effect of Jardiance (empagliflozin) on exercise ability and heart failure symptoms in people with chronic heart failure

EMPERIAL is part of the most comprehensive clinical trial program of an SGLT2 inhibitor in chronic heart failure

RIDGEFIELD, Conn. and INDIANAPOLIS, March 6, 2018 /PRNewswire/ -- Boehringer Ingelheim and Eli Lilly and Company (NYSE: LLY) today announced plans to expand their clinical trial program for Jardiance® in chronic heart failure with the EMPERIAL clinical trials. These trials will evaluate the effect of Jardiance on exercise ability and heart failure symptoms in people with chronic heart failure independent of whether they have type 2 diabetes. EMPERIAL comprises two Phase III trials that will assess the effect of 12 weeks of treatment with Jardiance on the ability of people with heart failure to perform daily exercise.

The plans for the EMPERIAL trials follow initiation of the EMPEROR trials in March 2017. While the EMPEROR outcome trials focus on long-term morbidity and mortality outcomes in people with heart failure, the EMPERIAL functional trials will investigate possible benefits on exercise capacity and heart failure symptoms. These studies are based on data obtained from the landmark EMPA-REG OUTCOME® trial, where the effect of Jardiance on heart failure outcomes was evaluated.

"Symptoms of heart failure can have a profound effect on quality of life, with more than three-quarters of people with heart failure finding it difficult to carry out routine activities," said Jeff Emmick, M.D., Ph.D., vice president, Product Development, Lilly Diabetes. "Currently, there are limited treatment options that can help improve the everyday lives of people living with chronic heart failure. We look forward to seeing whether Jardiance can help address this unmet need."

Heart failure is a serious condition where the heart is unable to pump enough blood around the body. It affects 26 million people worldwide, including more than 6 million Americans, and is associated with high morbidity and mortality. Approximately 50 percent of people who develop heart failure die within five years, and it is a leading cause of hospitalization in the United States and Europe.

"Boehringer Ingelheim and Lilly are committed to exploring how Jardiance can improve patient health outcomes and fill treatment gaps to serve as a broad cardiometabolic treatment option," said Thomas Seck, M.D., vice president of Clinical Development and Medical Affairs – Primary Care, Boehringer Ingelheim Pharmaceuticals, Inc. "We were encouraged by the heart failure findings with Jardiance in the EMPA-REG OUTCOME trial and look forward to the additional data from our other ongoing trials."

About EMPERIAL

EMPERIAL consists of two Phase III randomized, double-blind trials. The trials evaluate the effect of 12 weeks' treatment of once-daily Jardiance 10 mg compared with placebo on exercise ability and heart failure symptoms in patients with chronic heart failure with preserved or reduced ejection fraction.* This will be measured by the 6-minute walk test, a common measure of functional exercise capacity.

- **EMPERIAL-preserved** [[NCT03448406](#)]: will investigate Jardiance in patients with chronic heart failure with preserved ejection fraction (HFpEF). The study looks at a functional endpoint — how far patients can walk in 6 minutes — and a heart failure symptoms.
 - Primary endpoint: Change from baseline to week 12 in exercise capacity as measured by the distance walked in 6 minutes
 - Anticipated number of patients: approx. 300
 - Estimated completion: 2019
- **EMPERIAL-reduced** [[NCT03448419](#)]: will investigate Jardiance in patients with chronic heart failure with reduced ejection fraction (HFrEF). The study looks at a functional endpoint — how far patients can walk in 6 minutes — and at heart failure symptoms.
 - Primary endpoint: Change from baseline to week 12 in exercise capacity as measured by the distance walked in 6 minutes
 - Anticipated number of patients: approx. 300
 - Estimated completion: 2019

***Ejection fraction** is a measurement of the percentage of blood leaving the heart each time it contracts. During each heartbeat pumping cycle, the

heart contracts and relaxes. When the heart contracts, it ejects blood from the two pumping chambers (ventricles). When the heart relaxes, the ventricles refill with blood.

HFpEF occurs when the heart muscle contracts normally but the ventricle muscles are stiff. They do not relax as they should when the ventricle fills with blood, so less blood can enter the heart compared to a normally functioning heart.

HFrEF occurs when the heart muscle does not contract effectively and less blood is pumped out to the body compared to a normally functioning heart. Both HFpEF and HFrEF lead to similar symptoms of heart failure, specifically difficulty breathing, swelling and fatigue.

About Heart Failure

Heart failure is a progressive, debilitating and potentially fatal condition that occurs when the heart cannot pump enough blood around the body. Symptoms of heart failure include difficulty breathing, swelling — most commonly in feet, legs and ankles — and fatigue, among others. Heart failure is a prevalent disease; 26 million people around the world and more than 6 million people in the United States have chronic heart failure. There is a high unmet need in the treatment of heart failure, as approximately 50 percent of people diagnosed with heart failure will die within five years. Additionally, heart failure represents the most common cause of hospitalization among individuals aged 65 years and over in the United States and Europe. Heart failure is highly prevalent in people with diabetes, but approximately half of all people with heart failure do not have diabetes.

What is JARDIANCE? (www.jardiance.com)

JARDIANCE is a prescription medicine used along with diet and exercise to lower blood sugar in adults with type 2 diabetes.

JARDIANCE is also used to reduce the risk of cardiovascular death in adults with type 2 diabetes who have known cardiovascular disease.

JARDIANCE is not for people with type 1 diabetes or for people with diabetic ketoacidosis (increased ketones in the blood or urine).

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.

- **Ketoacidosis (increased ketones in your blood or urine).** Ketoacidosis is a serious condition and may need to be treated in the hospital. Ketoacidosis may lead to death. Ketoacidosis occurs in people with type 1 diabetes and can also occur in people with type 2 diabetes taking JARDIANCE, even if blood sugar is less than 250 mg/dL. **Stop taking JARDIANCE and call your doctor right away if you get any of the following symptoms**, and if possible, check for ketones in your urine:

- nausea
- vomiting
- stomach-area (abdominal) pain
- tiredness
- trouble breathing

- **Serious urinary tract infections.** Serious urinary tract infections can occur in people taking JARDIANCE and may lead to hospitalization. Tell your doctor if you have symptoms of a urinary tract infection such as a burning feeling when passing urine, a need to urinate often or right away, pain in the lower part of your stomach or pelvis, or blood in the urine. Sometimes people also may have a fever, back pain, nausea or vomiting.
- **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.

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
- are going to have surgery
- are eating less due to illness, surgery, or a change in your diet
- have or have had problems with your pancreas, including pancreatitis or surgery on your pancreas
- drink alcohol very often, or drink a lot of alcohol in the short term ("binge" drinking)
- have any other medical conditions
- are pregnant or plan to become pregnant. JARDIANCE may harm your unborn baby. Tell your doctor right away if you become pregnant during treatment with JARDIANCE.
- are breastfeeding, or plan to breastfeed. JARDIANCE may pass into your breast milk and may harm your baby. Do not breastfeed while taking JARDIANCE.

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 heartbeat
 - Sweating
 - Shaking or feeling jittery
- **Kidney problems.** Sudden kidney injury has happened in people taking JARDIANCE. Talk to your doctor right away if you reduce the amount you eat or drink, or if you lose liquids; for example, from vomiting, diarrhea, or being in the sun too long.
- **Allergic (hypersensitivity) reactions.** Symptoms of serious allergic reactions to JARDIANCE may include:
 - swelling of your face, lips, throat and other areas of your skin
 - difficulty with swallowing or breathing
 - raised, red areas on your skin (hives)

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

- **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](#) and [Patient Information](#).

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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. This alliance leverages the strengths of two of the world's leading pharmaceutical companies. By joining forces, the companies demonstrate commitment in the care of patients 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 Boehringer Ingelheim

Boehringer Ingelheim Pharmaceuticals, Inc., based in Ridgefield, CT, is the largest U.S. subsidiary of Boehringer Ingelheim Corporation.

Boehringer Ingelheim is one of the world's top 20 pharmaceutical companies. Headquartered in Ingelheim, Germany, the company operates globally

with approximately 50,000 employees. Since its founding in 1885, the company has remained family-owned and today creates value through innovation for three business areas including human pharmaceuticals, animal health and biopharmaceutical contract manufacturing.

Boehringer Ingelheim is committed to improving lives and providing valuable services and support to patients and their families. Our employees create and engage in programs that strengthen our communities. Please visit our [website](#) to learn more about how we make more health for more people through our Corporate Social Responsibility initiatives.

In 2016, Boehringer Ingelheim achieved net sales of about \$17.6 billion (15.9 billion euros). R&D expenditure corresponds to 19.6 percent of its net sales.

For more information please visit www.boehringer-ingelheim.us, or follow us on Twitter @BoehringerUS.

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 wide range of therapies 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 and newsroom.lilly.com/social-channels.

This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about the expansion of clinical trials to evaluate Jardiance as a treatment for adults with heart failure and reflects Lilly's current belief. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of development and commercialization. Among other things, there can be no guarantee that future study results will be consistent with the results to date or that Jardiance will receive additional regulatory approvals. For further discussion of these and other risks and uncertainties, see Lilly's most recent Form 10-K and Form 10-Q filings with the United States Securities and Exchange Commission. Except as required by law, Lilly undertakes no duty to update forward-looking statements to reflect events after the date of this release.

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SOURCE Eli Lilly and Company; Boehringer Ingelheim