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Jardiance® reduced risk of cardiovascular death in adults with type 2 diabetes and peripheral artery disease

- Jardiance (empagliflozin) reduced the risk of cardiovascular death by 43 percent versus placebo in patients with type 2 diabetes and peripheral artery disease**
- In a population at high risk for amputations, no increased risk in lower-limb amputation was observed with Jardiance treatment**

RIDGEFIELD, Conn. and INDIANAPOLIS, Nov. 13, 2017 /PRNewswire/ -- New data presented today showed that Jardiance® reduced the risk of cardiovascular death compared with placebo when added to standard of care in adults with type 2 diabetes and peripheral artery disease. These results, from a post-hoc analysis of the landmark EMPA-REG OUTCOME® trial, were shared as an oral presentation on behalf of Boehringer Ingelheim and Eli Lilly and Company (NYSE: LLY) at the American Heart Association® (AHA) Scientific Sessions 2017 in Anaheim, Calif. and simultaneously published online in the AHA's journal, *Circulation*.

"Peripheral artery disease, one of the most common cardiovascular complications associated with type 2 diabetes, increases the risk of death from cardiovascular causes," said Subodh Verma, M.D., cardiac surgeon-scientist at St. Michael's Hospital and professor at the University of Toronto. "There is an urgent need for treatment options that can improve cardiovascular-related outcomes in people with type 2 diabetes and peripheral artery disease."

Approximately one in three people with diabetes over the age of 50 has peripheral artery disease, a narrowing of the arteries outside the heart, usually those leading to the arms, legs and feet, due to a buildup of fatty deposits. Peripheral artery disease can be life-threatening when blockages restrict circulation, causing damage to limbs, and can also be associated with damage to vital organs such as the heart, kidneys and brain. If peripheral artery disease is not managed properly, it can also lead to amputation, which may result in hospitalization, disability and death.

At study start, 21 percent of the more than 7,000 EMPA-REG OUTCOME trial participants had existing peripheral artery disease. The analysis in this patient population showed that compared with placebo, on top of standard of care:

- | Jardiance reduced the risk of cardiovascular death by 43 percent
- | Death from any cause was reduced by 38 percent and hospitalization for heart failure by 44 percent
- | Risk for the composite endpoint of cardiovascular death, non-fatal heart attack or non-fatal stroke was reduced by 16 percent
- | New or worsening kidney disease, known as nephropathy, was reduced by 46 percent
- | Overall, the cardiovascular and renal effects observed in patients with peripheral artery disease were consistent with previously reported results of the overall trial population in EMPA-REG OUTCOME

Overall side effects and serious side effects were balanced between the Jardiance and placebo groups in adults with and without peripheral artery disease. In the group with peripheral artery disease, lower-limb amputations occurred in 5.5 percent of those treated with Jardiance and 6.3 percent of those treated with placebo. In the group without peripheral artery disease, lower-limb amputations occurred in 0.9 percent of those treated with Jardiance and 0.7 percent of those treated with placebo.

"Through ongoing sub-analyses of the EMPA-REG OUTCOME data, we are gaining a better understanding of how Jardiance may help a wide range of people living with type 2 diabetes and its complications," said Rogelio Braceras, M.D., therapeutic area head, Clinical Development & Medical Affairs, Metabolism, Boehringer Ingelheim Pharmaceuticals, Inc. "The data presented and published at the AHA Scientific Sessions showed that Jardiance reduced the risk for cardiovascular death and kidney disease in this highly vulnerable population of people with type 2 diabetes and peripheral artery disease."

Jardiance is the first and only oral type 2 diabetes medicine approved to reduce the risk of cardiovascular death in adults with type 2 diabetes and established cardiovascular disease.

About Diabetes and Cardiovascular Disease

Approximately 30 million Americans and an estimated 415 million people worldwide have diabetes, and nearly 24 percent of Americans with diabetes—or more than 7 million people—are undiagnosed. In the U.S., approximately nine percent of those aged 18 and older have diabetes. Type 2 diabetes is the most common type, accounting for an estimated 90 to 95 percent of all diagnosed adult diabetes cases in the U.S. Diabetes is a chronic condition that occurs when the body does not properly produce or use the hormone insulin.

Due to the complications associated with diabetes, such as high blood sugar, high blood pressure and obesity, cardiovascular disease is a major complication and the leading cause of death associated with diabetes. People with diabetes are two to four times more likely to develop cardiovascular disease than people without diabetes. Approximately 50 percent of deaths in people with type 2 diabetes worldwide and approximately two-thirds of deaths in people with type 2 diabetes in the U.S. are caused by cardiovascular disease. In the U.S., healthcare costs for managing cardiovascular conditions in patients with diabetes totaled more than \$23 billion in 2012.

Having a history of diabetes at age 60 can shorten a person's lifespan by as much as six years compared with someone without diabetes. And having both diabetes and a history of heart attack or stroke at age 60 can shorten a person's lifespan by as much as 12 years compared with someone without these conditions.

About the EMPA-REG OUTCOME Trial ([NCT01131676](#))

EMPA-REG OUTCOME was a long-term, multicenter, randomized, double-blind, placebo-controlled trial of more than 7,000 patients from 42 countries with type 2 diabetes and established cardiovascular disease.

The study assessed the effect of Jardiance (10 mg or 25 mg once daily) added to standard of care compared with placebo added to standard of care. Standard of care was comprised of glucose-lowering agents and cardiovascular drugs (including for blood pressure and cholesterol). The primary endpoint was defined as time to first occurrence of cardiovascular death, non-fatal heart attack or non-fatal stroke.

The overall safety profile of Jardiance was consistent with that of previous trials.

About Educational Initiatives

Given the critical connection between diabetes and cardiovascular disease, Boehringer Ingelheim and Eli Lilly and Company are committed to providing a wide range of diabetes therapies along with programs and support to raise awareness, understanding and action toward reducing the impact of cardiovascular disease in people with type 2 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:

- 1 **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:

- 1 have low blood pressure
- 1 take medicines to lower your blood pressure including water pills (diuretics)
- 1 are on a low salt diet
- 1 have kidney problems
- 1 are 65 years of age or older.

- 1 **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. 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
- | 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 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 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.

| **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 Jardiance 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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View original content with multimedia: <http://www.prnewswire.com/news-releases/jardiance-reduced-risk-of-cardiovascular-death-in-adults-with-type-2-diabetes-and-peripheral-artery-disease-300554785.html>

SOURCE Eli Lilly and Company; Boehringer Ingelheim

