# Jardiance® decreased relative risk of hospitalization for heart failure by 50% versus DPP-4 inhibitors and by 30% versus GLP-1 receptor agonists in adults with type 2 diabetes in real-world evidence study

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- *Jardiance showed a reduction in relative risk of all-cause mortality by 40% compared with DPP-4 inhibitors in the subset of people with Medicare coverage*
- *Data from these final analyses of EMPRISE complements findings from the landmark EMPA-REG OUTCOME® trial*

RIDGEFIELD, Conn. and INDIANAPOLIS, June 5, 2022 /PRNewswire/ -- Two analyses of the final U.S. data from the EMPagliflozin compaRative effectIveness and SafEty (EMPRISE) real-world study show that Jardiance® (empagliflozin) was associated with a reduction in risk of hospitalization for heart failure compared with two other classes of glucose-lowering therapies in adults with type 2 diabetes in routine care. Relative risk reductions were 50% versus dipeptidyl peptidase-4 (DPP-4) inhibitors and 30% versus glucagon-like peptide 1 (GLP-1) receptor agonists. The results were presented on behalf of Boehringer Ingelheim and Eli Lilly and Company (NYSE: LLY) at the American Diabetes Association Scientific Sessions 2022 in New Orleans.

"With more than 29 million people in the U.S. diagnosed with type 2 diabetes, up to 22% of whom may also have heart failure, it is critical that healthcare professionals caring for this population have treatments that demonstrate cardiovascular effectiveness in routine care," said Elisabetta Patorno, M.D., Dr.P.H., Division of Pharmacoepidemiology and Pharmacoeconomics, Brigham and Women's Hospital and associate professor of medicine, Harvard Medical School, and study co-investigator. "These five-year results from EMPRISE, showing empagliflozin was associated with a decreased risk of hospitalization for heart failure and for death, are encouraging data for adults with type 2 diabetes and their care team."

Compared with DPP-4 inhibitors, Jardiance was also associated with a 40% reduction in relative risk of all-cause mortality in people who had Medicare. In the overall EMPRISE population, Jardiance was associated with a 12% reduction in the risk of the composite outcome of myocardial infarction or stroke compared with DPP-4 inhibitors.

Compared with GLP-1 receptor agonists, Jardiance was associated with similar risks of heart attack, stroke and all-cause mortality. All results for Jardiance compared with GLP-1 receptor agonists, and with liraglutide (a GLP-1 receptor agonist) specifically, were consistent for people with and without cardiovascular disease.

Results from the EMPRISE real-world study, which assessed the first five years of use of Jardiance in the U.S., complement previously reported data from the landmark EMPA-REG OUTCOME® trial, in which Jardiance showed a 35% relative risk reduction in hospitalization for heart failure compared with placebo in adults with type 2 diabetes and established cardiovascular disease. EMPA-REG OUTCOME also showed a 38% relative risk reduction in cardiovascular death with Jardiance versus placebo.

"People with type 2 diabetes are four times as likely to be hospitalized for heart failure, and repeated hospitalizations lead to worse outcomes, making treatment options that improve clinical outcomes crucial," said Mohamed Eid, M.D., M.P.H., M.H.A., vice president, Clinical Development & Medical Affairs, Cardio-Metabolism & Respiratory Medicine, Boehringer Ingelheim Pharmaceuticals, Inc. "These findings suggest that treatment with Jardiance can help reduce heart failure hospitalizations compared to other classes of diabetes therapies, with a well-understood safety and tolerability profile."

The EMPRISE findings confirmed the well-established safety profile of Jardiance. Compared with DPP-4 inhibitors, Jardiance was associated with a reduction in relative risk of acute kidney injury. There was an increase in relative risk of hospitalization for diabetic ketoacidosis, which is consistent with Jardiance's known safety information. Risks for lower-limb amputations, fractures and renal and bladder cancers were similar.

"We are pleased to present the final data from EMPRISE in the U.S., which encompasses information from nearly 500,000 adults in a real-world care setting," said Leonard Glass, M.D., F.A.C.E., vice president of Diabetes Global Medical Affairs, Lilly. "As we strive to help fill unmet treatment needs, this study reinforces our longstanding commitment to people living with cardio-metabolic conditions. Building upon our robust clinical trial program, EMPRISE highlights the potential of Jardiance to improve health outcomes in routine clinical practice."

**About EMPRISE**
EMPRISE was initiated in 2016 to complement the EMPA-REG OUTCOME trial results by providing data on the comparative effectiveness and safety of Jardiance in routine clinical care versus DPP-4 inhibitors or GLP-1 receptor agonists.

The final analyses of EMPRISE U.S. data assessed the first five years of Jardiance use in nearly 500,000 adults with type 2 diabetes, with and without cardiovascular disease, in the U.S. between 2014 and 2019: the first included more than 230,000 adults who initiated either Jardiance or a DPP-4 inhibitor (115,116 adults in each treatment arm); the second included more than 260,000 adults who initiated either Jardiance or a GLP-1 receptor agonist (130,408 adults in each treatment arm).

Additional EMPRISE studies including Asia and Europe will provide insights from different regions of the world with an international perspective on the use of Jardiance in routine clinical care.

EMPRISE U.S. was initiated and led by academic researchers from the Division of Pharmacoepidemiology at Brigham and Women's Hospital and Harvard Medical School, Boston. The study is part of an academic collaboration between Brigham and Women's Hospital and Boehringer Ingelheim.

**Prioritizing Cardio-Renal-Metabolic Care**
Through research and educational initiatives, Boehringer Ingelheim and Lilly are driven to redefine care for people with cardio-renal-metabolic conditions, a group of interconnected disorders that affect more than one billion people worldwide and are a leading cause of death.

The cardiovascular, renal (kidney) and metabolic systems are closely intertwined and share many of the same disease-related pathways. Dysfunction in one system may accelerate the onset of dysfunction in others, resulting in the progression of comorbid diseases such as type 2 diabetes, heart failure and chronic kidney disease. Conversely, improving the health of one system can lead to positive effects across the others and can help reduce the risk for further complications.

Understanding their interconnected nature, we are working to advance treatments for people with cardio-renal-metabolic conditions. It is only through a holistic approach to care that we can truly transform outcomes and restore the harmony among these critical systems.

**What is JARDIANCE?**

JARDIANCE is a prescription medicine used to:

- reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure, when the heart cannot pump enough blood to the rest of your body
- reduce the risk of cardiovascular death in adults with type 2 diabetes who also have known cardiovascular disease
- lower blood sugar along with diet and exercise in adults with type 2 diabetes

JARDIANCE is not for people with type 1 diabetes. It may increase their risk of diabetic ketoacidosis (increased ketones in the blood or urine).

JARDIANCE is not for use to lower blood sugar in adults with type 2 diabetes who have severe kidney problems, because it may not work.

**IMPORTANT SAFETY INFORMATION**

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

**Do not take** JARDIANCE if you are on dialysis.

**JARDIANCE can cause serious side effects, including:**

- **Ketoacidosis (increased ketones in your blood or urine).** Ketoacidosis is a serious condition which needs 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**. Ketoacidosis has also happened in people with diabetes who were sick or who had surgery during treatment with JARDIANCE. **Stop taking JARDIANCE and call your healthcare provider right away or go to the nearest hospital emergency room 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

- **Dehydration. JARDIANCE** can cause some people to become dehydrated (the loss of body water and salt). Dehydration may cause you to feel dizzy, faint, light-headed, or weak, especially when you stand up. Sudden worsening of kidney function has happened in people who are taking JARDIANCE.

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

    - 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

  Talk to your healthcare provider about what you can do to prevent dehydration, including how much fluid you should drink on a daily basis, and if you reduce the amount of food or liquid you drink, if you are sick or cannot eat, or start to lose liquids from your body from vomiting, diarrhea, or being in the sun too long.

- **Serious urinary tract infections.** Serious urinary tract infections can occur in people taking JARDIANCE and may lead to hospitalization. Tell your healthcare provider 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.

- **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

- **Necrotizing fasciitis. A rare but serious bacterial infection that causes damage to the tissue under the skin in the area between and around your anus and genitals (perineum).** This bacterial infection has happened in women and men who take JARDIANCE, and may lead to hospitalization, multiple surgeries, and death. **Seek medical attention immediately if you have fever or are feeling very weak, tired or uncomfortable (malaise), and you develop any of the following symptoms in the area between and around your anus and genitals: pain or tenderness, swelling, and redness of skin (erythema).**

- **Vaginal yeast infection.** Talk to your healthcare provider if you have 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.** Swelling of an uncircumcised penis may develop that makes it difficult to pull back the skin around the tip of the penis. Talk to your healthcare provider if you have redness, itching or swelling of the penis, rash of the penis, foul smelling discharge from the penis, and/or pain in the skin around the penis.

  **Talk to your healthcare provider about what to do if you get symptoms of a yeast infection of the vagina or penis**. Your healthcare provider may suggest you use an over-the-counter antifungal medicine. Talk to your healthcare provider right away if you use an over-the-counter antifungal medication and your symptoms do not go away.

- **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 healthcare provider or go to the nearest emergency room right away.

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

These are not all the possible side effects of JARDIANCE. For more information, ask your healthcare provider or pharmacist.

**Before taking JARDIANCE, tell your healthcare provider about all of your medical conditions, including if you:**

- have kidney problems
- have liver problems
- have a history of infection of the vagina or penis
- have a history of urinary tract infections or problems with urination
- are going to have surgery. Your healthcare provider may stop your JARDIANCE before you have surgery. Talk to your healthcare provider if you are having surgery about when to stop taking JARDIANCE and when to start it again
- are eating less or there is 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 type 1 diabetes. JARDIANCE should not be used to treat people with type 1 diabetes
- are pregnant or plan to become pregnant. JARDIANCE may harm your unborn baby. Tell your healthcare provider right away if you become pregnant during treatment with JARDIANCE
- are breastfeeding or are planning to breastfeed. JARDIANCE may pass into your breast milk and may harm your baby. Do not breastfeed while taking JARDIANCE

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

**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 Prescribing Information and Medication Guide.

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**Boehringer Ingelheim and Eli Lilly and Company**
In January 2011, Boehringer Ingelheim and Eli Lilly and Company announced an Alliance that centers on compounds representing several of the largest diabetes treatment classes. Depending on geographies, the companies either co-promote or separately promote the respective molecules each contributing to the Alliance. The Alliance leverages the strengths of two of the world's leading pharmaceutical companies to focus on patient needs. By joining forces, the companies demonstrate their commitment, not only to the care of people with diabetes, but also to investigating the potential to address areas of unmet medical need.

**About Lilly**
Lilly unites caring with discovery to create medicines that make life better for people around the world. We've been pioneering life-changing discoveries for nearly 150 years, and today our medicines help more than 47 million people across the globe. Harnessing the power of biotechnology, chemistry and genetic medicine, our scientists are urgently advancing new discoveries to solve some of the world's most significant health challenges, redefining diabetes care, treating obesity and curtailing its most devastating long-term effects, advancing the fight against Alzheimer's disease, providing solutions to some of the most debilitating immune system disorders, and transforming the most difficult-to-treat cancers into manageable diseases. With each step toward a healthier world, we're motivated by one thing: making life better for millions more people. That includes delivering innovative clinical trials that reflect the diversity of our world and working to ensure our medicines are accessible and affordable. To learn more, visit lilly.com and lilly.com/newsroom or follow us on Facebook, Instagram, Twitter and LinkedIn.

**About Boehringer Ingelheim**
Making new and better medicines for humans and animals is at the heart of what we do. Our mission is to create breakthrough therapies that change lives. Since its founding in 1885, Boehringer Ingelheim is independent and family-owned. We have the freedom to pursue our long-term vision, looking ahead to identify the health challenges of the future and targeting those areas of need where we can do the most good.

As a world-leading, research-driven pharmaceutical company, with around 52,000 employees, we create value through innovation daily for our three business areas: Human Pharma, Animal Health, and Biopharmaceutical Contract Manufacturing. In 2020, Boehringer Ingelheim achieved net sales of around 22.33 billion USD (19.57 billion EUR). Our significant investment of over 4.2 billion USD (3.7 billion EUR) in 2020 (18.9% of net sales) in R&D drives innovation, enabling the next generation of medicines that save lives and improve quality of life.

We realize more scientific opportunities by embracing the power of partnership and diversity of experts across the life-science community. By working together, we accelerate the delivery of the next medical breakthrough that will transform the lives of patients now, and in generations to come.

Boehringer Ingelheim Pharmaceuticals, Inc., based in Ridgefield, CT, is the largest U.S. subsidiary of Boehringer Ingelheim Corporation and is part of the Boehringer Ingelheim group of companies. In addition, there are Boehringer Ingelheim Animal Health in Duluth, GA and Boehringer Ingelheim Fremont, Inc. in Fremont, CA.

Boehringer Ingelheim is committed to improving lives and strengthening our communities. Please visit www.boehringer-ingelheim.us/csr to learn more about Corporate Social Responsibility initiatives.

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

*This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about Jardiance as a treatment for adults with type 2 diabetes, to reduce the risk of cardiovascular death in adults with type 2 diabetes and known cardiovascular disease, and to reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure, and as a potential treatment for adults with cardio-renal-metabolic conditions and reflects Lilly's current beliefs and expectations. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of drug research, development and commercialization. Among other things, there can be no guarantee that planned or ongoing studies will be completed as planned, that future study results will be consistent with the results to date or that Jardiance will receive additional regulatory approvals. For a further discussion of these and other risks and uncertainties that could cause actual results to differ from Lilly's expectations, please see Lilly's most recent Forms 10-K and 10-Q filed with the U.S. Securities and Exchange Commission. Lilly undertakes no duty to update forward-looking statements.*



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