US FDA approves Jardiance® for the treatment of adults with chronic kidney disease

September 22, 2023

- *Approval adds to the treatment options for the more than 35 million adults in the U.S. affected by chronic kidney disease (CKD)*
- *Jardiance® (empagliflozin) 10 mg tablets significantly reduced the risk of kidney disease progression and cardiovascular death in adults with CKD, as established in the EMPA-KIDNEY phase III trial*
- *EMPA-KIDNEY is the first SGLT2 inhibitor CKD trial to demonstrate a statistically significant reduction in the risk of first and recurrent hospitalization in adults with CKD*

RIDGEFIELD, Conn. and INDIANAPOLIS, Sept. 22, 2023 /PRNewswire/ -- The U.S. Food and Drug Administration (FDA) has approved Jardiance® (empagliflozin) 10 mg tablets to reduce the risk of sustained decline in estimated glomerular filtration rate (eGFR), end-stage kidney disease, cardiovascular death and hospitalization in adults with chronic kidney disease (CKD) at risk of progression, Boehringer Ingelheim and Eli Lilly and Company (NYSE: LLY) announced.

Jardiance is not recommended for use to improve glycemic control in patients with type 1 diabetes. It may increase the risk of diabetic ketoacidosis in these patients. Jardiance is not recommended for use to improve glycemic control in patients with type 2 diabetes with an eGFR less than 30 mL/min/1.73 m^2. Jardiance is likely to be ineffective in this setting based upon its mechanism of action. Jardiance is not recommended for the treatment of chronic kidney disease in patients with polycystic kidney disease or patients requiring or with a recent history of intravenous immunosuppressive therapy or greater than 45 mg of prednisone or equivalent for kidney disease. Jardiance is not expected to be effective in these populations.

"This approval provides healthcare professionals in the U.S. with another treatment option for adults with CKD that can reduce the risk of kidney function decline, kidney failure, cardiovascular death and hospitalizations," said Katherine Tuttle, M.D., Executive Director for Research, Providence Inland Northwest Health, Regional Principal investigator for the Institute of Translational Health Sciences and Professor of Medicine at the University of Washington, and EMPA-KIDNEY steering committee member. "The meaningful benefits that empagliflozin demonstrated in the EMPA-KIDNEY phase III trial are welcome news for adults living with CKD in this country."

"CKD affects more than one in seven adults in the U.S., 90% of whom are undiagnosed, and it remains a significantly under-recognized public health crisis," said Mohamed Eid, M.D., M.P.H., M.H.A., vice president, Clinical Development & Medical Affairs, Cardio-Renal-Metabolism & Respiratory Medicine, Boehringer Ingelheim Pharmaceuticals, Inc. "Hospitalizations account for a third to a half of total healthcare costs for this population, and disease progression often leads to serious cardiovascular complications and kidney failure, which can require dialysis or transplantation. Given the clinically demonstrated benefits of Jardiance, we are proud to now be able to offer this option to adults with CKD at risk for progression."

Jardiance is contraindicated in people with hypersensitivity to empagliflozin or any of the excipients in Jardiance, as reactions such as angioedema have occurred. **Please see additional Important Safety Information below.**

EMPA-KIDNEY was a large trial designed to reflect the broad range of adults with CKD with or without type 2 diabetes. Based on the trial inclusion/exclusion criteria, over 6,600 patients were enrolled. Patients included had an eGFR ≥20 to <45 mL/min/1.73 m^2 or an eGFR ≥45 to <90 mL/min/1.73 m^2 with a urine albumin to creatinine ratio ≥200 mg/g. Included patients were deemed appropriate for treatment with an SGLT2 inhibitor by a local investigator. Patients were excluded if they had both type 2 diabetes and prior atherosclerotic cardiovascular disease with eGFR above 60 mL/min/1.73 m^2, had type 1 diabetes, had a functioning or scheduled kidney transplant, were on dialysis, had polycystic kidney disease, or required or had a recent history of intravenous immunosuppressive therapy or greater than 45 mg of prednisone or equivalent for kidney disease.

In EMPA-KIDNEY, Jardiance demonstrated a 28% relative risk reduction (absolute risk reduction 3.6% per patient-year at risk, HR=0.72; 95% CI 0.64 to 0.82; P<0.0001) compared with placebo, both on top of standard care, for the composite primary endpoint of kidney disease progression* or cardiovascular death. The event rate for Jardiance was 13.1% (432/3304) and for placebo was 16.9% (558/3305). EMPA-KIDNEY is the first SGLT2 inhibitor CKD trial to demonstrate a significant reduction in the risk of first and recurrent hospitalization, a pre-specified key secondary endpoint, with a 14% relative risk reduction (HR=0.86; 95% CI 0.78 to 0.95; p=0.0025) with Jardiance versus placebo. In the Jardiance group, 1,611 hospitalizations occurred among 960 patients (24.8 events per 100 patient-years). In the placebo group, 1,895 hospitalizations occurred among 1,035 patients (29.2 events per 100 patient-years).

This milestone marks the fourth FDA approval for Jardiance stemming from the EMPOWER program. With more than 700,000 adults enrolled worldwide in clinical trials, EMPOWER reinforces the long-term commitment of the Boehringer Ingelheim and Lilly Alliance to improve outcomes for people living with cardio-renal-metabolic conditions.

"Following previous indications for Jardiance in heart failure and type 2 diabetes, this FDA approval now provides physicians, including nephrologists, with an important treatment option for adults living with CKD at risk for progression," said Leonard Glass, M.D., F.A.C.E., senior vice president, Diabetes Global Medical Affairs, Lilly. "Alongside the recent CKD approval for Jardiance in the EU, this decision further bolsters our efforts to support this community globally."

**Kidney disease progression: Defined as end-stage kidney disease (the initiation of maintenance dialysis or receipt of a kidney transplant), a sustained decline in estimated glomerular filtration rate (eGFR) to below 10 mL/min/1.73 m^2, kidney death or a sustained decline of at least 40% in eGFR from*

randomization).

About EMPA-KIDNEY
EMPA-KIDNEY (NCT03594110) is a multinational, randomized, double-blind, placebo-controlled clinical trial, designed to evaluate the effect of Jardiance on kidney disease progression and cardiovascular mortality risk. The primary outcome is defined as time to a first event of either cardiovascular death or kidney disease progression, defined as end-stage kidney disease (the need for kidney replacement therapy such as dialysis or kidney transplantation), a sustained decline in eGFR to <10 mL/min/1.73 m^2, kidney death or a sustained decline of ≥40% in eGFR from randomization. Key secondary outcomes include cardiovascular death or hospitalization for heart failure, all-cause hospitalization and all-cause mortality. EMPA-KIDNEY includes 6,609 adults from eight countries with CKD, both with and without diabetes, who were randomized to receive either Jardiance 10 mg or placebo, once daily, both on top of current standard of care.

Patients included had an eGFR ≥20 to <45 mL/min/1.73 m^2 or an eGFR ≥45 to <90 mL/min/1.73 m^2 with a urine albumin to creatinine ratio ≥200 mg/g. Included patients were deemed appropriate for treatment with an SGLT2 inhibitor by a local investigator. Patients were excluded if they had both type 2 diabetes and prior atherosclerotic cardiovascular disease with eGFR above 60 mL/min/1.73 m^2, had type 1 diabetes, had a functioning or scheduled kidney transplant, were on dialysis, had polycystic kidney disease, or required or had a recent history of intravenous immunosuppressive therapy or greater than 45 mg of prednisone or equivalent for kidney disease.

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 further worsening of kidney disease, end-stage kidney disease (ESKD), death due to cardiovascular disease, and hospitalization in adults with chronic kidney disease
- 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 and children who are 10 years of age and older with type 2 diabetes

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

JARDIANCE is not for people with polycystic kidney disease, or who are taking or have recently received certain types of immunosuppressive therapy to treat kidney disease. JARDIANCE is not expected to work if you have these conditions.

IMPORTANT SAFETY INFORMATION

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

Symptoms of a serious allergic reaction may include:

- rash
- raised, red areas on your skin (hives)
- swelling of your face, lips, mouth, and throat that may cause difficulty in breathing or swallowing

If you have any of these symptoms, stop taking JARDIANCE and call your healthcare provider right away or go to the nearest hospital emergency room.

JARDIANCE can cause serious side effects, including:

- **Diabetic ketoacidosis (increased ketones in your blood or urine) in people with type 1 and other ketoacidosis.** JARDIANCE can cause ketoacidosis that can be life-threatening and may lead to death. Ketoacidosis is a serious condition which needs to be treated in a hospital. People with type 1 diabetes have a high risk of getting ketoacidosis. People with type 2 diabetes or pancreas problems also have an increased risk of getting ketoacidosis. Ketoacidosis can also happen in people who are sick, cannot eat or drink as usual, skip meals, and are on a diet high in fat and low in carbohydrates (ketogenic diet), take less than the usual amount of insulin or miss insulin doses, drink too much alcohol, have a loss of too much fluid from the body (volume depletion), or who have surgery. Ketoacidosis can happen even if your blood sugar is less than 250 mg/dL. Your healthcare provider may ask you to periodically check ketones in your urine or blood. **Stop taking JARDIANCE and call your healthcare provider or get medical help right away if you get any of the following. If possible, check for ketones in your urine or blood, even if your blood sugar is less than 250 mg/dL:**
  - nausea
  - vomiting
  - stomach-area (abdominal) pain
  - tiredness
  - trouble breathing
  - ketones in your urine or blood

- **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. Call your healthcare provider right away 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.

- **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 skin around 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.

- **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): In adults, 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. In children 10 years of age and older, the risk for low blood sugar is higher with JARDIANCE regardless of use with another medicine that can also lower blood sugar. 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 people who take JARDIANCE, and may lead to hospitalization, multiple surgeries, and death. **Seek medical attention immediately if you have a 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).**
- **Amputations. SGLT2 inhibitors may increase your risk of lower limb amputations.** You may be at a higher risk of lower limb amputation if you:
    - have a history of amputation
    - have had blocked or narrowed blood vessels, usually in your leg
    - have had diabetic foot infection, ulcers or sores

Call your healthcare provider right away if you have new pain or tenderness, any sores, ulcers, or infections in your leg or foot. Talk to your healthcare provider about proper foot care.

- **Serious allergic reactions.** If you have any symptoms of a serious allergic reaction, stop taking JARDIANCE and call your healthcare provider right away or go to the nearest hospital emergency room.

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 type 1 diabetes or have had diabetic ketoacidosis
- have a decrease in your insulin dose
- have a serious infection
- have a history of infection of the vagina or penis
- have a history of amputation
- have kidney problems
- have liver problems
- have a history of urinary tract infections or problems with urination
- are on a low sodium (salt) diet. Your healthcare provider may change your diet or dose
- are going to have surgery. Your healthcare provider may stop 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
- are dehydrated
- 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 ever had an allergic reaction to JARDIANCE
- 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.

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.

CL-JAR-100168 09.21.2023

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 Boehringer Ingelheim
Boehringer Ingelheim is working on breakthrough therapies that transform lives, today and for generations to come. As a leading research-driven biopharmaceutical company, the company creates value through innovation in areas of high unmet medical need. Founded in 1885 and family-owned ever since, Boehringer Ingelheim takes a long-term, sustainable perspective. More than 53,000 employees serve over 130 markets in the two business units Human Pharma and Animal Health. Learn more at boehringer-ingelheim.com/us/

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 51 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.

Cautionary Statement Regarding Forward-Looking Statements
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, to reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure, as a treatment for children 10 years and older with type 2 diabetes, and as a treatment for adults with chronic kidney disease, 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 is no guarantee that planned or ongoing studies will be completed as planned, that future study results will be consistent with study results to date or that Jardiance® will receive additional regulatory approvals. For further discussion of these and other risks and uncertainties that could cause actual results to differ from Lilly's expectations, see Lilly's 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.

Jardiance® is a registered trademark of Boehringer Ingelheim.

P-LLY
MPR-US-102857

CONTACTS:

Sheryl van der Hilst
Boehringer Ingelheim
Email: sheryl.van_der_hilst@boehringer-ingelheim.com
Phone: (914) 772-7973

Kristiane Bello
Eli Lilly and Company
Email: bello_kristiane@lilly.com
Phone: (317) 315-9052

View original content to download multimedia:https://www.prnewswire.com/news-releases/us-fda-approves-jardiance-for-the-treatment-of-adults-with-chronic-kidney-disease-301936176.html

SOURCE Eli Lilly and Company