US FDA accepts supplemental New Drug Application for Jardiance® for adults with chronic kidney disease

January 20, 2023

The supplemental New Drug Application is based on results from the landmark EMPA-KIDNEY phase III trial, which showed Jardiance® (empagliflozin) tablets significantly reduced the risk of kidney disease progression or cardiovascular death in adults with CKD by 28% (absolute risk reduction [ARR]: 3.8%) compared with placebo, both on top of standard of care.*

RIDGEFIELD, Conn. and INDIANAPOLIS, Jan. 20, 2023 /PRNewswire/ -- The U.S. Food and Drug Administration (FDA) has accepted a supplemental New Drug Application (sNDA) for Jardiance® (empagliflozin) tablets, which is being investigated as a potential treatment to reduce the risk of kidney disease progression and cardiovascular death in adults with chronic kidney disease (CKD), Boehringer Ingelheim and Eli Lilly and Company (NYSE: LLY) announced.

"There is a significant need for additional therapies that reduce the risk of kidney disease progression and hospitalizations in adults with CKD," 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. "This application acceptance is an important step forward for the approximately 37 million people in the U.S. living with CKD."

The sNDA is based on results from the landmark EMPA-KIDNEY phase III trial, in which Jardiance significantly reduced the risk of kidney disease progression* or cardiovascular death in adults with CKD by 28% (ARR: 3.8%) compared with placebo, both on top of standard of care. Results were presented during the American Society of Nephrology (ASN)'s Kidney Week 2022 and simultaneously published in *The New England Journal of Medicine*. EMPA-KIDNEY is the first SGLT2 inhibitor CKD trial to show a significant reduction in risk of hospitalization for any cause, with a 14% relative risk reduction with Jardiance versus placebo (24.8 vs. 29.2 events/100 patient-years, respectively), both on top of standard of care, in a pre-specified key secondary endpoint. Reductions in other key secondary endpoints of hospitalization for heart failure or cardiovascular death or all-cause death were not statistically significant. Hospitalizations account for 35% to 55% of total healthcare costs for people with CKD in the U.S.

EMPA-KIDNEY, the largest and broadest dedicated SGLT2 inhibitor trial in CKD to date, provides additional data for patients commonly seen in clinical practice. The trial enrolled 6,609 participants, including people without diabetes (56%), those with various underlying causes of CKD and those across the spectrum of eGFR and urine albumin-creatinine ratio (measures of kidney function and excess albumin in the urine, respectively). Overall, the safety data in EMPA-KIDNEY were consistent with the previously known safety profile of Jardiance.

Initially approved in 2014, Jardiance is a once-daily tablet used along with diet and exercise to lower blood sugar in adults with type 2 diabetes; and to reduce the risk of cardiovascular death in adults with type 2 diabetes and known cardiovascular disease. Jardiance is also indicated to reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure. Jardiance is not for patients with type 1 diabetes, or to improve glycemic control in adults with type 2 diabetes with an eGFR <30 mL/min/1.73 m^2. Jardiance is contraindicated in people with hypersensitivity to empagliflozin or any of the excipients in Jardiance, and in patients on dialysis. **Please see additional Important Safety Information below.**

"This marks another exciting milestone for Jardiance, potentially extending its ability to positively impact the approximately one billion people diagnosed with a cardio, renal or metabolic condition," said Jeff Emmick, M.D., Ph.D., vice president, Product Development, Lilly. "We look forward to working with the FDA during the review process and eagerly await a decision later this year on the indication for CKD, which doubles a person's risk for hospitalization."

In March 2020, the FDA granted Fast Track designation to the clinical investigation of Jardiance to reduce the risk of kidney disease progression and cardiovascular death in adults with CKD. According to the FDA, Fast Track designation is designed to facilitate the development of drugs and expedite treatments that may address serious conditions and fill an unmet medical need. Jardiance is not indicated for the treatment of CKD.

**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: The study of heart and kidney protection with Jardiance
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 percent 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 randomized from eight countries with established CKD both with and without diabetes, as well as with and without albuminuria, receiving either Jardiance 10 mg or placebo, on top of current standard of care.

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 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).**

- **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 JARDIANCE before you have surgery. Talk to your healthcare provider about when to stop taking JARDIANCE if you are having surgery 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.

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 Boehringer Ingelheim
Boehringer Ingelheim is working on breakthrough therapies that improve the lives of humans and animals. 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 perspective. Around 52,000 employees serve more than 130 markets in the three business areas, Human Pharma, Animal Health, and Biopharmaceutical Contract Manufacturing. Learn more at www.boehringer-ingelheim.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 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 and LinkedIn.

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-kidney-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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View original content to download multimedia:https://www.prnewswire.com/news-releases/us-fda-accepts-supplemental-new-drug-application-for-jardiance-for-adults-with-chronic-kidney-disease-301726873.html

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