

# JARDIANCE INITIATION GUIDE

## PROVEN BENEFITS FOR PATIENTS



### Lifesaving CV benefit

to reduce the risk of CV death for adults with type 2 diabetes and established CV disease

Reductions in CV death were seen in patients with and without a prior CV event.<sup>1\*</sup>

Please see following pages for study designs and additional study data.



### Significantly reduced A1C

for adults with T2D, along with diet and exercise

As add-on to metformin, JARDIANCE demonstrated a mean A1C reduction up to 0.8%, from baseline 7.9% vs placebo.



### Significantly reduced weight

for adults with T2D, along with diet and exercise

As add-on to metformin, JARDIANCE demonstrated a mean weight reduction up to 5.2 lbs (2.9%) from baseline 180 lbs vs placebo.

JARDIANCE is not indicated for weight loss. Weight change was a secondary endpoint.<sup>2</sup>

## How to administer JARDIANCE



**10 MG**

The recommended dose of JARDIANCE is 10 mg once daily, taken orally in the morning, with or without food.



**25 MG**

In patients who tolerate JARDIANCE 10 mg, the dose can be increased to 25 mg once daily.

Reductions in risk of CV death were consistent for both dosing strengths.

No dose adjustment needed in patients with eGFR  $\geq 45$  mL/min/1.73 m<sup>2</sup>.

## How to administer JARDIANCE (continued)

- In patients with volume depletion, correcting this condition prior to initiation of JARDIANCE is recommended
- **Dosing in patients with renal impairment:**
  - Assessment of renal function is recommended prior to initiation of JARDIANCE and periodically thereafter
  - Should not be initiated if eGFR is  $< 45$  mL/min/1.73 m<sup>2</sup>
  - Should be discontinued if eGFR is persistently  $< 45$  mL/min/1.73 m<sup>2</sup>
  - Reduction in risk of CV death was consistently observed among patients, including those with eGFR  $< 60$  mL/min/1.73 m<sup>2</sup>

## INDICATIONS AND LIMITATIONS OF USE

JARDIANCE is indicated to reduce the risk of cardiovascular (CV) death in adults with type 2 diabetes mellitus and established CV disease.

JARDIANCE is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

JARDIANCE is not recommended for patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.

## IMPORTANT SAFETY INFORMATION

**CONTRAINDICATIONS:** History of serious hypersensitivity to empagliflozin or any of the excipients in JARDIANCE; severe renal impairment, end-stage renal disease, or dialysis.

## WARNINGS AND PRECAUTIONS

**Hypotension:** Empagliflozin causes intravascular volume contraction and symptomatic hypotension may occur. Before initiating JARDIANCE, assess and correct volume status in the elderly, and in patients with renal impairment, low systolic blood pressure, or on diuretics. Monitor for hypotension.

## Things your patient should know



### Stay hydrated

Due to the mechanism of action, JARDIANCE could cause increased urination and dehydration. Blood pressure-lowering medicines or diuretics the patient is taking may need to be reduced, in order to lower the risk of dehydration.



### Maintain genital hygiene

The most common adverse events were urinary tract and yeast infections in women. Proper hygiene is key to prevention for men and women. Inform your patients of symptoms to watch out for, so they can help you recognize a potential infection early and treat appropriately.<sup>3,4</sup>



### Diet and exercise

Maintain a balanced diet and exercise regimen when taking JARDIANCE.

## How to administer JARDIANCE (continued)

- A lower dose of insulin or insulin secretagogues (eg, sulfonylureas) may be required to reduce the risk of hypoglycemia when JARDIANCE is used in combination with these agents
- JARDIANCE is contraindicated in patients with a history of serious hypersensitivity to empagliflozin or any of the excipients in JARDIANCE; severe renal impairment, end-stage renal disease, or dialysis

**Ketoacidosis:** Ketoacidosis, a serious life-threatening condition requiring urgent hospitalization, has been identified in patients with type 1 and type 2 diabetes mellitus receiving SGLT2 inhibitors, including empagliflozin. Fatal cases of ketoacidosis have been reported in patients taking empagliflozin. Patients who present with signs and symptoms of metabolic acidosis should be assessed for ketoacidosis, even if blood glucose levels are less than 250 mg/dL. If suspected, discontinue JARDIANCE, evaluate, and treat promptly. Before initiating JARDIANCE, consider risk factors for ketoacidosis. Patients may require monitoring and temporary discontinuation in situations known to predispose to ketoacidosis.

Please see following pages for Important Safety Information. Please see [Prescribing Information](#) and [Medication Guide](#).

\*Established CV disease consisted of peripheral artery disease, coronary artery disease, or a history of MI or stroke.<sup>3</sup>

CV=cardiovascular;  
eGFR=estimated glomerular  
filtration rate; MI=myocardial  
infarction; SGLT2=sodium  
glucose co-transporter-2  
inhibitor; T2D=type 2 diabetes.

**Jardiance**<sup>®</sup>  
(empagliflozin) tablets  
10 mg/25 mg

For additional information,  
your patients can [visit JARDIANCE.com](http://JARDIANCE.com)

**Jardiance**<sup>®</sup>   
(empagliflozin) tablets  
10 mg/25 mg

## INDICATIONS AND LIMITATIONS OF USE

JARDIANCE is indicated to reduce the risk of cardiovascular (CV) death in adults with type 2 diabetes mellitus and established CV disease.

JARDIANCE is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

JARDIANCE is not recommended for patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.

## IMPORTANT SAFETY INFORMATION

**CONTRAINDICATIONS:** History of serious hypersensitivity to empagliflozin or any of the excipients in JARDIANCE; severe renal impairment, end-stage renal disease, or dialysis.

### WARNINGS AND PRECAUTIONS

**Hypotension:** Empagliflozin causes intravascular volume contraction and symptomatic hypotension may occur. Before initiating JARDIANCE, assess and correct volume status in the elderly, and in patients with renal impairment, low systolic blood pressure, or on diuretics. Monitor for hypotension.

**Ketoacidosis:** Ketoacidosis, a serious life-threatening condition requiring urgent hospitalization, has been identified in patients with type 1 and type 2 diabetes mellitus receiving SGLT2 inhibitors, including empagliflozin. Fatal cases of ketoacidosis have been reported in patients taking empagliflozin. Patients who present with signs and symptoms of metabolic acidosis should be assessed for ketoacidosis, even if blood glucose levels are less than 250 mg/dL. If suspected, discontinue JARDIANCE, evaluate, and treat promptly. Before initiating JARDIANCE, consider risk factors for ketoacidosis. Patients may require monitoring and temporary discontinuation in situations known to predispose to ketoacidosis.

**Acute Kidney Injury and Impairment in Renal Function:** Empagliflozin causes intravascular volume contraction and can cause renal impairment. Acute kidney injury requiring hospitalization and dialysis have been identified in patients taking SGLT2 inhibitors, including empagliflozin; some reports involved patients younger than 65 years of age. Before initiating JARDIANCE, consider factors that may predispose patients to acute kidney injury. Consider temporary discontinuation in settings of reduced oral intake or fluid losses. Monitor patients for signs and symptoms of acute kidney injury. If it occurs, discontinue JARDIANCE and treat promptly.

Empagliflozin increases serum creatinine and decreases eGFR. Patients with hypovolemia may be more susceptible to these changes. Before initiating JARDIANCE, evaluate renal function and monitor thereafter. More frequent monitoring is recommended in patients with eGFR <60 mL/min/1.73 m<sup>2</sup>. Discontinue JARDIANCE in patients with a persistent eGFR <45 mL/min/1.73 m<sup>2</sup>.

**Urosepsis and Pyelonephritis:** Serious urinary tract infections including urosepsis and pyelonephritis requiring hospitalization have been identified in patients receiving SGLT2 inhibitors, including empagliflozin. Treatment with SGLT2 inhibitors increases the risk for urinary tract infections. Evaluate for signs and symptoms of urinary tract infections and treat promptly.

**Hypoglycemia:** The use of JARDIANCE in combination with insulin or insulin secretagogues can increase the risk of hypoglycemia. A lower dose of insulin or the insulin secretagogue may be required.

**Necrotizing Fasciitis of the Perineum (Fournier's Gangrene):** Serious, life-threatening cases have occurred in both females and males. Assess patients presenting with pain or tenderness, erythema, or swelling in the genital or perineal area, along with fever or malaise. If suspected, institute prompt treatment and discontinue JARDIANCE.

**Genital Mycotic Infections:** Empagliflozin increases the risk for genital mycotic infections, especially in patients with prior infections. Monitor and treat as appropriate.

**Hypersensitivity Reactions:** Discontinue JARDIANCE, treat promptly, and monitor until signs and symptoms resolve.

**Increased Low-Density Lipoprotein Cholesterol (LDL-C):** Monitor and treat as appropriate.

**MOST COMMON ADVERSE REACTIONS (≥5%):** Urinary tract infections and female genital mycotic infections.

**DRUG INTERACTIONS:** Coadministration with diuretics may enhance the potential for volume depletion.

### USE IN SPECIAL POPULATIONS

**Pregnancy:** JARDIANCE is not recommended, especially during the second and third trimesters.

**Lactation:** JARDIANCE is not recommended while breastfeeding.

**Geriatric Use:** JARDIANCE is expected to have diminished efficacy in elderly patients with renal impairment. Renal function should be assessed more frequently in elderly patients. The incidence of volume depletion-related adverse reactions and urinary tract infections increased in patients ≥75 years treated with empagliflozin.

CL-JAR-100023 10.30.18

Please see [Prescribing Information](#) and [Medication Guide](#).

**EMPA-REG OUTCOME Trial design:** A randomized, double-blind, parallel-group trial comparing the risk of experiencing a major adverse cardiovascular event between JARDIANCE and placebo when these were added to and used concomitantly with standard of care treatments for type 2 diabetes and cardiovascular disease. A total of 7020 patients were treated (JARDIANCE 10 mg [N=2345]; JARDIANCE 25 mg [N=2342]; placebo [N=2333]) and followed for a median of 3.1 years. All patients had established atherosclerotic cardiovascular disease at baseline, including one or more of the following: a documented history of coronary artery disease, peripheral artery disease, myocardial infarction, or stroke. The primary outcome was reduction in risk of cardiovascular events, defined by the composite of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke.

**EMPA-REG OUTCOME Trial (primary composite endpoint results):** JARDIANCE demonstrated a **14% RRR** (HR=0.86 [95% CI: 0.74-0.99]; p=0.04). The absolute risk reduction for the composite endpoint was **1.6%**. There was no change in risk of nonfatal MI (HR=0.87 [95% CI: 0.70-1.09]) or nonfatal stroke (HR=1.24 [95% CI: 0.92-1.67]); the 14% RRR in CV events was due to a reduction in the risk of CV death (HR=0.62 [95% CI: 0.49-0.77]).

**Post-hoc analysis of EMPA-REG OUTCOME Trial—reduction in risk of CV death across CVD subgroups:** CV death was analyzed in subgroups by type of CV disease at baseline. Differences between treatment groups were assessed using Cox regression analysis in patients treated with  $\geq 1$  dose of study drug. The post-hoc analysis was not designed to determine statistical significance.<sup>1</sup>

**Rate of CV death (%) across CVD subgroups from EMPA-REG OUTCOME Trial:** All values depict JARDIANCE vs placebo, respectively. With PAD, 4.5 vs 7.5; without, 3.5 vs 5.5. With CAD, 3.7 vs 5.8; without, 3.8 vs 5.9. With history of MI, 4.6 vs 7.6; without, 2.8 vs 4.4. With history of stroke, 4.3 vs 8.0; without, 3.5 vs 5.2.<sup>1</sup>

**Add-on to metformin study design:** A Phase III, randomized, double-blind, placebo-controlled, parallel-group, efficacy and safety study of JARDIANCE (10 mg, 25 mg) administered orally once daily over 24 weeks in patients with type 2 diabetes mellitus with insufficient glycemic control despite treatment with metformin  $\geq 1500$  mg alone. Six hundred thirty-seven treated patients received placebo + metformin (N=207), JARDIANCE 10 mg + metformin (N=217), or JARDIANCE 25 mg + metformin (N=213). The primary endpoint was A1C change from baseline. Weight change and blood pressure change from baseline were secondary endpoints.<sup>6</sup>

**A1C change results from the add-on to metformin study:** Mean reduction in A1C up to 0.8% from baseline of 7.9%. Adjusted mean changes of -0.1% from baseline 7.9% for placebo, -0.7% from baseline 7.9% for JARDIANCE 10 mg, and -0.8% for JARDIANCE 25 mg, respectively. Difference from placebo (adjusted mean) was -0.6% for both JARDIANCE 10 mg and 25 mg; p<0.0001 vs placebo.

**Weight change results from the add-on to metformin study:** Mean reduction in weight up to 5.2 lbs (2.9%) from baseline of 180 lbs. Adjusted mean changes of -0.5% reduction in body weight (-0.9 lbs) from baseline 176 lbs for placebo, -2.5% (-4.5 lbs) from baseline 180 lbs for JARDIANCE 10 mg, and -2.9% (-5.2 lbs) from baseline 180 lbs for JARDIANCE 25 mg, respectively; p<0.0001 vs placebo. **JARDIANCE is not indicated for weight loss.**

CI=confidence interval; HR=hazard ratio; RRR=relative risk reduction.

**References:** **1.** Data on file. Boehringer Ingelheim Pharmaceuticals, Inc. **2.** Roden M, Weng J, Eilbracht J, et al; EMPA-REG MONO Trial Investigators. *Lancet Diabetes Endocrinol.* 2013;1(3):208-219. **3.** Urinary Tract Infection. Centers for Disease Control and Prevention, National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), Division of Healthcare Quality Promotion (DHQP). [www.cdc.gov/antibiotic-use/community/for-patients/common-illnesses/uti.html#prevention](http://www.cdc.gov/antibiotic-use/community/for-patients/common-illnesses/uti.html#prevention). Accessed February 7, 2019. **4.** What Are Yeast Infections? Urology Care Foundation. [www.urologyhealth.org/urologic-conditions/yeast-infections](http://www.urologyhealth.org/urologic-conditions/yeast-infections). Accessed February 7, 2019. **5.** Zinman B, Wanner C, Lachin JM, et al; EMPA-REG OUTCOME Investigators. *N Engl J Med.* 2015;373(22):2117-2128. **6.** Häring HU, Merker L, Seewaldt-Becker E, et al; EMPA-REG MET Trial Investigators. *Diabetes Care.* 2014;37(6):1650-1659.

Please see [Prescribing Information](#) and [Medication Guide](#).

## JARDIANCE HAS BEST-IN-CLASS COMMERCIAL COVERAGE<sup>1\*†</sup>

After initiating JARDIANCE, ensure your patients leave with the following resources



### JARDIANCE Savings Card

Allows your patients to pay as little as \$0<sup>†</sup> every month for an entire year if they qualify

Please see below for full terms and conditions.



### Patient Education Brochure

A helpful reference for patients to learn more about JARDIANCE

\*Source: Fingertip Formulary, health plan or state listed above, and/or data on file, Boehringer Ingelheim Pharmaceuticals, Inc. as of 3/1/2019. Percentage of covered lives represent a weighted average of both commercial and Part D availability.<sup>1</sup>

†Placement on formulary does not establish clinical comparability of products, including safety and efficacy, and is not a guarantee of full or partial coverage and/or payment. Contact health plan, state, or www.medicare.gov for most current information, as it may change without notice. This is not intended to be an exhaustive list of all plans in your area. Boehringer Ingelheim Pharmaceuticals, Inc. and Lilly USA, LLC does not sponsor or endorse any particular plan, and the company/plan names listed do not imply their endorsement of Boehringer Ingelheim Pharmaceuticals, Inc., Lilly USA, LLC, or the product(s) referenced. Boehringer Ingelheim Pharmaceuticals, Inc. either owns or uses the trademark JARDIANCE® under license. Other referenced trademarks are owned by third parties.

**Terms & Conditions:** Eligible commercially insured patients 18 years or older may pay as little as \$0/month with a maximum savings up to \$250 per 30-day supply. Benefits not to exceed program expiration on December 31, 2019. If you live in Massachusetts, voucher expires on the earlier of December 31, 2019, or date AB rated generic equivalent is available. Other state restrictions may apply. One card per patient, not transferable, and cannot be combined with any other offer. **Card not accepted in Veteran's Affairs pharmacies.** Program not health insurance. You must present this card to the pharmacist with your JARDIANCE prescription to participate. Only valid for commercially insured patients in the 50 United States, DC, and Puerto Rico. **Offer not valid for patients without commercial coverage or patients whose prescriptions for JARDIANCE are eligible to be reimbursed, in whole or in part, by any governmental program such as Medicaid, Medicare or any state patient or pharmaceutical assistance program** and where prohibited by law. Offer may change at any time, without notice.

## IMPORTANT SAFETY INFORMATION (continued)

### WARNINGS AND PRECAUTIONS (continued)

**Acute Kidney Injury and Impairment in Renal Function:** Empagliflozin causes intravascular volume contraction and can cause renal impairment. Acute kidney injury requiring hospitalization and dialysis have been identified in patients taking SGLT2 inhibitors, including empagliflozin; some reports involved patients younger than 65 years of age. Before initiating JARDIANCE, consider factors that may predispose patients to acute kidney injury. Consider temporary discontinuation in settings of reduced oral intake or fluid losses. Monitor patients for signs and symptoms of acute kidney injury. If it occurs, discontinue JARDIANCE and treat promptly.

Empagliflozin increases serum creatinine and decreases eGFR. Patients with hypovolemia may be more susceptible to these changes. Before initiating JARDIANCE, evaluate renal function and monitor thereafter. More frequent monitoring is recommended in patients with eGFR <60 mL/min/1.73 m<sup>2</sup>. Discontinue JARDIANCE in patients with a persistent eGFR <45 mL/min/1.73 m<sup>2</sup>.

**Urosepsis and Pyelonephritis:** Serious urinary tract infections including urosepsis and pyelonephritis requiring hospitalization have been identified in patients receiving SGLT2 inhibitors, including empagliflozin. Treatment with SGLT2 inhibitors increases the risk for urinary tract infections. Evaluate for signs and symptoms of urinary tract infections and treat promptly.

**Hypoglycemia:** The use of JARDIANCE in combination with insulin or insulin secretagogues can increase the risk of hypoglycemia. A lower dose of insulin or the insulin secretagogue may be required.

**Necrotizing Fasciitis of the Perineum (Fournier's Gangrene):** Serious, life-threatening cases have occurred in both females and males. Assess patients presenting with pain or tenderness, erythema, or swelling in the genital or perineal area, along with fever or malaise. If suspected, institute prompt treatment and discontinue JARDIANCE.

Please see additional Important Safety Information on previous pages. Please see [Prescribing Information](#) and [Medication Guide](#).