Jardiance®
(empagliflozin) tablets
10 mg/25 mg

JARDIANCE

CV OUTCOME TRIAL

Zinman B, Wanner C, Lachin JM, et al; EMPA-REG OUTCOME Investigators. *N Engl J Med*. 2015;373(22):2117-2128.

INDICATION 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 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.

Please see additional Important Safety Information on following pages. Please see Prescribing Information and Medication Guide.

CV=cardiovascular.

JARDIANCE CV Outcome Trial[1]

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OBJECTIVE

To investigate the effects of JARDIANCE, compared to placebo, on time to first occurrence of CV death, nonfatal myocardial infarction, or nonfatal stroke in patients with one or more cardiovascular risk factors (including coronary artery disease, peripheral artery disease, history of myocardial infarction, or history of stroke) and type 2 diabetes.

STUDY DESIGN

A total of 7020 patients with established CV disease and type 2 diabetes were treated in a multicenter, double-blind, placebo-controlled trial. The median observation time was 3.1 years.

- Inclusion criteria were BMI ≤45 kg/m^2, established cardiovascular disease, A1C ≥7% to <9% for patients not receiving glucose-lowering therapy for 12 weeks before randomization, and A1C ≥7% to <10% for patients receiving stable glucose-lowering therapy for 12 weeks before randomization
- Eligible patients were randomized to receive placebo (N=2333), JARDIANCE 10 mg (N=2345), or JARDIANCE 25 mg (N=2342)
- Exclusion criteria included: uncontrolled hyperglycemia (glucose level >13.3 mmol/L [240 mg/dL]) after an overnight fast; indication of liver disease; planned cardiac surgery or angioplasty within 3 months of starting treatment; estimated glomerular filtration rate <30 mL/min/1.73 m^2 at screening or during run-in; bariatric surgery; treatment with anti-obesity drugs

STANDARD OF CARE

Results were achieved on top of standard of care CV and glucose-lowering medications.

- Investigators were encouraged to treat other cardiovascular risk factors (including dyslipidemia and hypertension) to achieve the best available standard of care according to local guidelines
- Investigators were encouraged to adjust glucose-lowering therapy at their discretion to achieve glycemic control according to local guidelines, after 12 weeks

PRIMARY COMPOSITE ENDPOINT

- Time to first occurrence of cardiovascular events, defined by the composite of cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke

RESULTS

JARDIANCE resulted in a significantly lower risk of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke as compared with placebo.

- The primary outcome occurred in a significantly lower percentage of patients in the JARDIANCE group (10.5%) than in the placebo group (12.1%) (p=0.04). There was no change in nonfatal myocardial infarction or nonfatal stroke

STUDY CONCLUSIONS

JARDIANCE reduced the risk of CV death on top of standard of care.

- Patients with type 2 diabetes at high risk for cardiovascular events who received JARDIANCE, as compared with placebo, had a lower rate of the primary composite cardiovascular outcome and of cardiovascular death when the study drug was added to standard of care

IMPORTANT SAFETY INFORMATION (continued)
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^2. Discontinue JARDIANCE in patients with a persistent eGFR <45 mL/min/1.73 m^2.

Please see additional Important Safety Information on following pages. Please see Prescribing Information and Medication Guide.

For adults with T2D and established CV disease

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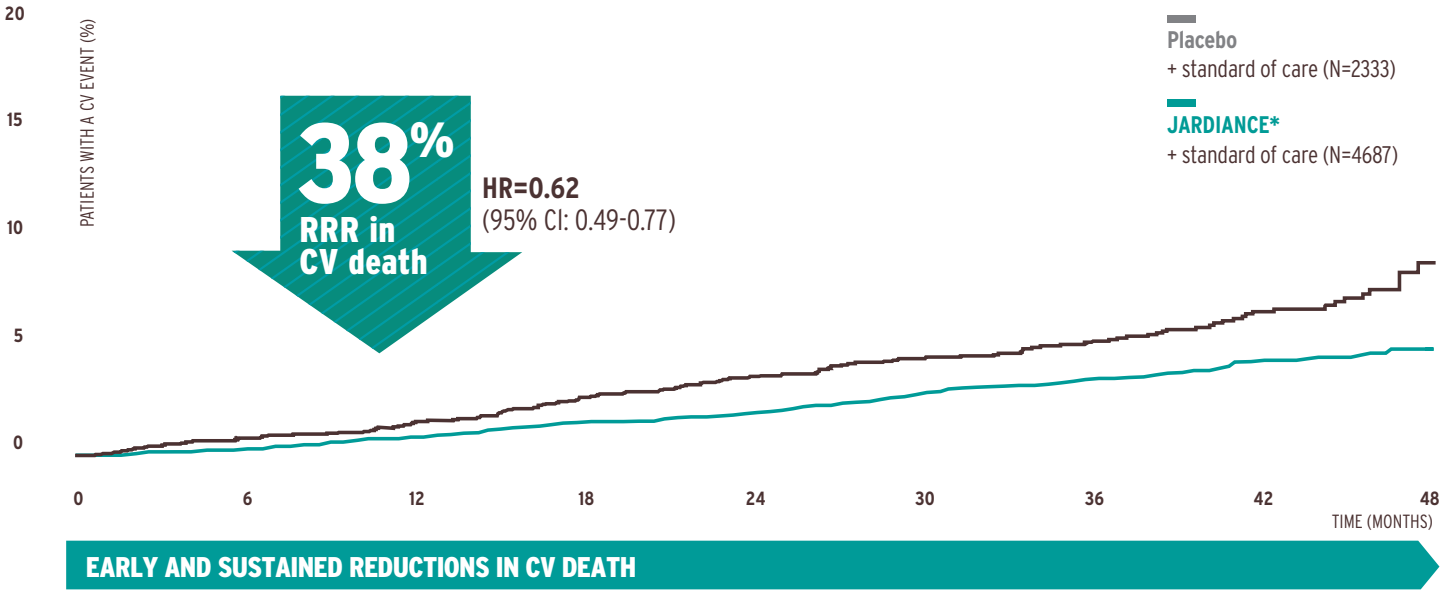
JARDIANCE significantly reduced the risk of CV death vs placebo[1]

A consistent finding for the two JARDIANCE dosing strengths, 10 mg and 25 mg



EARLY AND SUSTAINED REDUCTIONS IN CV DEATH

ABSOLUTE RATES FOR CV DEATH **5.9%** placebo **VS** **3.7%** JARDIANCE **2.2%** **ABSOLUTE RISK REDUCTION**

JARDIANCE DEMONSTRATED A 14% RRR FOR THE PRIMARY COMPOSITE ENDPOINT

(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])**

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

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.

*Pooled data from JARDIANCE 10 mg and JARDIANCE 25 mg; similar magnitude of reduction was shown with both doses.
CI=confidence interval; HR=hazard ratio; MI=myocardial infarction; RRR=relative risk reduction.

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Learn more about the lifesaving CV benefit of JARDIANCE at JARDIANCEhcp.com

View EMPA REG Outcomes Trial Results ▸

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IMPORTANT SAFETY INFORMATION (continued)
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.

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Reference: 1. Zinman B, Wanner C, Lachin JM, et al; EMPA-REG OUTCOME Investigators. *N Engl J Med.* 2015;373(22):2117-2128.

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