FIGHT FOR THEIR LIVES
NOW MORE THAN EVER

Jardiance®
(empagliflozin) tablets
10 mg/25 mg

CV DEATH CAN STRIKE ADULTS WITH ESTABLISHED CV DISEASE AND TYPE 2 DIABETES AT ANY TIME [1]

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.

CV=cardiovascular.

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 the following pages. Click to view accompanying Prescribing Information and Patient Information.

FOR ADULTS WITH ESTABLISHED CV DISEASE AND TYPE 2 DIABETES

JARDIANCE provided an additional reduction in the risk of CV death beyond standard of care[2]

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PATIENTS WERE ACTIVELY MANAGED WITH STANDARD OF CARE MEDICATIONS*

CARDIOVASCULAR MEDICATIONS

- ACEIs/ARBs
- Aspirin
- Statins
- Beta Blockers

TYPE 2 DIABETES MEDICATIONS

- Metformin
- Insulin
- SUs
- DPP-4 Inhibitors
- GLP-1 Agonists
- TZDs

AFTER ADDING JARDIANCE

38% RRR IN CV DEATH

2.2% ARR†

HR=0.62
(95% CI: 0.49-0.77)

PRIMARY COMPOSITE ENDPOINT

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]).

*Type 2 diabetes medications were kept stable for the first 12 weeks.
†Absolute rates for CV death: 5.9% placebo + standard of care vs 3.7% JARDIANCE + standard of care. Pooled data from JARDIANCE 10 mg and JARDIANCE 25 mg; similar magnitude of reduction was shown with both doses.

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.

Please see additional Important Safety Information on the following pages. Click to view accompanying Prescribing Information and Patient Information.

Please see last page for Trial Design.

ACEIs=angiotensin-converting enzyme inhibitors; ARBs=angiotensin II receptor blockers; ARR=absolute risk reduction; CI=confidence interval; DPP=dipeptidyl peptidase; GLP=glucagon-like peptide; HR=hazard ratio; MI=myocardial infarction; RRR=relative risk reduction; SU=sulfonylurea; TZD=thiazolidinedione.

Reduced risk of CV death was generally consistent across A1C subgroups[3‡]

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POST-HOC ANALYSIS: RATE OF CV DEATH FOR JARDIANCE AND PLACEBO ACROSS A1C SUBGROUPS

A1C AT BASELINE	RATE OF CV DEATH (%)	
	PLACEBO (N=2333)	JARDIANCE (N=4687)
<7.0%	7.9	2.4
7.0% – <8.0%	6.1	3.7
8.0% – <9.0%	5.4	3.7
≥9.0%	5.5	4.2

CHANGE IN A1C FROM BASELINE (MEDIAN 3.1 YEARS)	RATE OF CV DEATH (%)	
	PLACEBO (N=2333)	JARDIANCE (N=4687)
Reduction of ≥0.3%	6.7	3.7
Reduction of <0.3% or increase	5.3	3.6

Post-hoc Analysis: Risk of CV death was analyzed in the placebo and pooled JARDIANCE groups according to baseline A1C and change in A1C from baseline to the last value in the trial. A Cox proportional hazards model was used to assess the differences between the treatment groups. The post-hoc analysis was not designed to determine statistical significance.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

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 the following pages. Click to view accompanying Prescribing Information and Patient Information.

‡A pre-specified analysis included subgroups of patients with A1C <8.5% and ≥8.5%.

FOR ADULTS WITH ESTABLISHED CV DISEASE AND TYPE 2 DIABETES

In the EMPA-REG Outcome Trial, reduced risk of CV death was demonstrated in patients with established CV disease and T2D[3*]

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POST-HOC ANALYSIS: REDUCTION IN RISK OF CV DEATH WAS OBSERVED ACROSS CVD SUBGROUPS

- PERIPHERAL ARTERY DISEASE
- CORONARY ARTERY DISEASE
- HISTORY OF MI
- HISTORY OF STROKE

Post-hoc Analysis: 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 ≥1 dose of study drug. The post-hoc analysis was not designed to determine statistical significance.

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.

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.

Please see additional Important Safety Information on the following pages. Click to view accompanying Prescribing Information and Patient Information.

*Established CVD consisted of peripheral artery disease, coronary artery disease, or a history of MI or stroke.
CVD=cardiovascular disease; T2D=type 2 diabetes.

JARDIANCE demonstrated early and sustained reductions in CV death[2]

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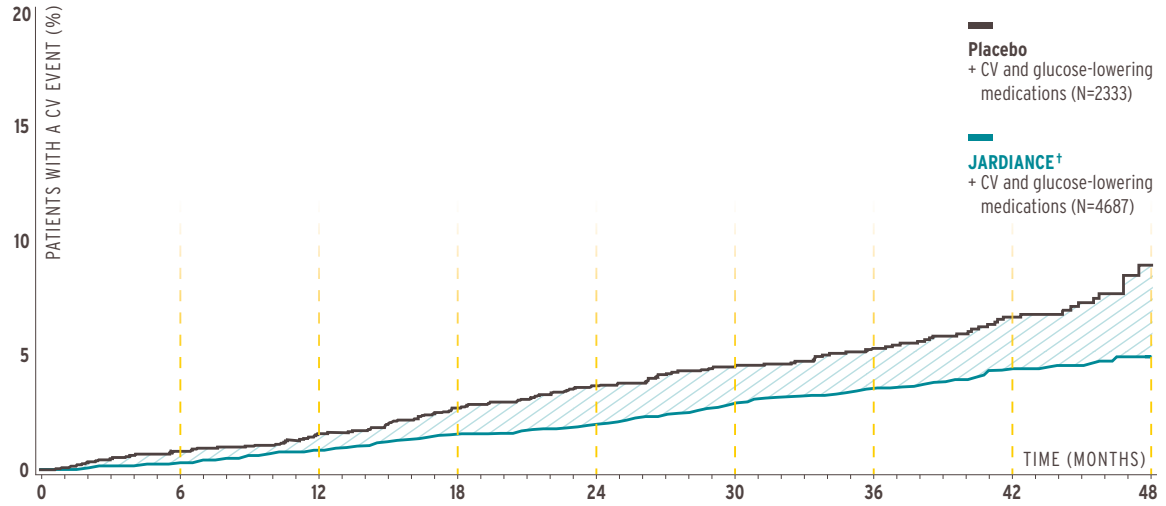

38% RRR IN CV DEATH
vs placebo on top of standard of care
HR=0.62 (95% CI: 0.49-0.77)

2.2% Absolute Risk Reduction

EARLY AND SUSTAINED REDUCTIONS IN CV DEATH[2]

CV DEATH CAN STRIKE AT ANY TIME.[1] PRESCRIBE JARDIANCE TODAY

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.

Please see additional Important Safety Information on the following pages. Click to view accompanying Prescribing Information and Patient Information.

†Pooled data from JARDIANCE 10 mg and JARDIANCE 25 mg; similar magnitude of reduction was shown with both doses.

Your colleagues are already prescribing JARDIANCE to reduce the risk of CV death.* WILL YOU?

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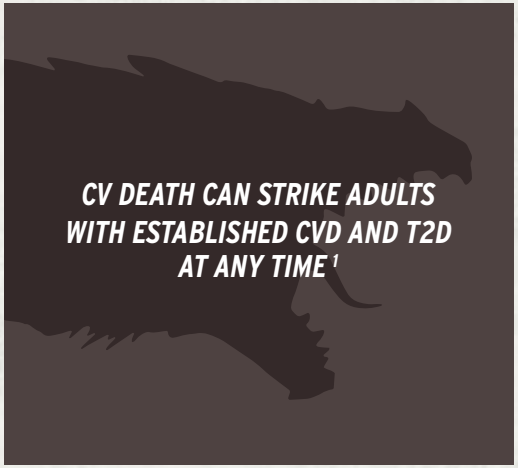

38%

RRR IN CV DEATH
vs placebo on top of standard of care

2.2% absolute risk reduction
HR=0.62 (95% CI: 0.49-0.77)

MOST INITIATED
by cardiologists, endocrinologists, and PCPs in its class*

IMPORTANT SAFETY INFORMATION (continued)

USE IN SPECIAL POPULATIONS (continued)

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-100004 12.19.17

JARDIANCE CV 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.

References: 1. National Institute of Diabetes and Digestive and Kidney Diseases, US Department of Health and Human Services. Bethesda, MD: National Institutes of Health; 2008. **2.** Zinman B, Wanner C, Lachin JM, et al; EMPA-REG OUTCOME Investigators. *N Engl J Med.* 2015;373(22):2117-2128. **3.** Data on file. Boehringer Ingelheim Pharmaceuticals, Inc.

Please see additional Important Safety Information on the previous pages. Click to view accompanying Prescribing Information and Patient Information.

*Source: IMS Health Diabetes NPA weekly files from 1/1/17 to 10/06/17. Based on NBRx (New to Brand Prescriptions) among physicians identified by specialty.

Boehringer Ingelheim

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