Jardiance®
(empagliflozin) tablets
10 mg/25 mg

FAQs

FOR CARDIOLOGISTS

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.

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

Jardiance® (empagliflozin) tablets 10 mg/25 mg

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.

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

Can diabetic ketoacidosis occur in patients treated with JARDIANCE?

The JARDIANCE Prescribing Information includes ketoacidosis in the Warnings and Precautions section.

Ketoacidosis (increased ketones in blood or urine) has been reported in patients treated with SGLT2 inhibitors, including JARDIANCE.[1]

For more information, please see additional Important Safety Information on page 2 and please see JARDIANCE Prescribing Information.

Jardiance® (empagliflozin) tablets 10 mg/25 mg

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^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. Please see Jardiance Prescribing Information and Medication Guide.

What is the mechanism of action (MOA) for JARDIANCE?

Sodium glucose co-transporter 2 (SGLT2) is the predominant transporter responsible for reabsorption of glucose from the glomerular filtrate back into the circulation. JARDIANCE contains empagliflozin, an SGLT2 inhibitor.

By inhibiting SGLT2, JARDIANCE reduces renal reabsorption of filtered glucose and lowers the renal threshold for glucose, and thereby increases urinary glucose excretion.

Patients should stay hydrated as the MOA of JARDIANCE can cause increased urination and dehydration.

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STUDY DESIGNS

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.

Monotherapy: A Phase III, randomized, double-blind, placebo-controlled, parallel-group, efficacy and safety study of JARDIANCE (10 mg, 25 mg) administered orally over 24 weeks in drug-naïve patients with type 2 diabetes mellitus and insufficient glycemic control despite diet and exercise. Six hundred seventy-six treated patients received placebo (N=228), JARDIANCE 10 mg (N=224), or JARDIANCE 25 mg (N=224). The primary endpoint was A1C change from baseline. Weight change and blood pressure change from baseline were secondary endpoints.[2]

Add-on to metformin: 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 ≥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.[3]

Please see additional study designs on page 8.

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.

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

Is there a risk of urinary tract infections (UTIs) and genital mycotic infections (GMIs) while taking JARDIANCE?

The most common adverse reactions associated with JARDIANCE (5% or greater incidence) were UTIs and female GMIs.

COMMON AEs IN EMPA-REG OUTCOME TRIAL[1]

	PLACEBO	JARDIANCE*
UTI	18.1%	18.0%
GMI	1.8%	6.4%

Proper hygiene and hydration are key to prevention for men and women. Inform patients of the potential for UTIs and GMIs, which may be serious. Advise your patient on symptoms, treatment options, and when to seek medical advice.[4,5]

For more information, please see additional Important Safety Information on page 6 and please see JARDIANCE Prescribing Information.

*Pooled data from JARDIANCE 10 mg and JARDIANCE 25 mg.[1]

ANSWER CONTINUED ON PAGE 9

Jardiance® (empagliflozin) tablets 10 mg/25 mg

STUDY DESIGNS

Add-on to metformin + SU: 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 ≥1500 mg in combination with an SU. Six hundred sixty-six treated patients received placebo + metformin + SU (N=225), JARDIANCE 10 mg + metformin + SU (N=225), or JARDIANCE 25 mg + metformin + SU (N=216). The primary endpoint was A1C change from baseline. Weight change from baseline was a secondary endpoint.[6]

Add-on to basal insulin ± orals: A randomized, double-blind, placebo-controlled, parallel-group, safety and efficacy study of JARDIANCE (10 mg, 25 mg) administered orally once daily over 78 weeks in patients with type 2 diabetes mellitus receiving treatment with basal insulin (eg, glargine, detemir, or NPH insulin) with or without concomitant metformin and/or an SU therapy, and insufficient glycemic control. Four hundred ninety-four treated patients received placebo (N=170), JARDIANCE 10 mg (N=169), or JARDIANCE 25 mg (N=155). The primary endpoint was A1C change from baseline after 18 weeks. Weight change from baseline was a secondary endpoint.[7]

Add-on to pioglitazone ± metformin: A randomized, double-blind, placebo-controlled, parallel-group, efficacy and safety trial 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 a background therapy of pioglitazone alone or in combination with metformin ≥1500 mg. Four hundred ninety-eight treated patients received placebo + pioglitazone (N=165), JARDIANCE 10 mg + pioglitazone (N=165), or JARDIANCE 25 mg + pioglitazone (N=168). The primary endpoint was A1C change from baseline. Weight change from baseline was a secondary endpoint.[8]

Please see additional study designs on page 6.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

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.

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

ANSWER CONTINUED FROM PAGE 7

Is there a risk of urinary tract infections (UTIs) and genital mycotic infections (GMIs) while taking JARDIANCE?

UTIs AND GMIs IN MONOTHERAPY AND COMBINATION THERAPY TRIALS*

	PLACEBO (N=995)	JARDIANCE 10 mg (N=999)	JARDIANCE 25 mg (N=977)
UTIs	**7.6%**	**9.3%**	**7.6%**
Males	3.2%	3.6%	4.1%
Females	16.6%	18.4%	17.0%
Female GMIs	**1.5%**	**5.4%**	**6.4%**
Male GMIs	**0.4%**	**3.1%**	**1.6%**

UTIs and GMIs were reported more often in patients with a history of chronic or recurrent UTIs or GMIs.

UTIs and GMIs were seen more frequently in females treated with JARDIANCE than in those treated with placebo.[1]

The incidence of UTIs in male patients was similar in males treated with JARDIANCE and with placebo.[1]

For more information, please see additional Important Safety Information on page 8 and please see JARDIANCE Prescribing Information.

*Adverse events, excluding hypoglycemia, reported in pooled, placebo-controlled clinical studies in ≥2% of patients treated with JARDIANCE and greater than placebo.

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IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

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.

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

Does JARDIANCE impact Low-Density Lipoprotein Cholesterol (LDL-C) levels?

JARDIANCE can cause increases in LDL-C. Monitor and treat as appropriate.

LDL-C increased by 2.3%, 4.6%, and 6.5% in patients treated with placebo, JARDIANCE 10 mg, and JARDIANCE 25 mg, respectively.

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IMPORTANT SAFETY INFORMATION (continued)

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

Can JARDIANCE be used with other oral antidiabetic medications?

JARDIANCE has been studied in combination with antidiabetic medications, such as metformin, dipeptidyl peptidase-4 (DPP-4) inhibitors, and insulin.

JARDIANCE is available in fixed-dose combinations with other type 2 diabetes medications.

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SELECT SAFETY INFORMATION

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.

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.

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

Does JARDIANCE have drug-drug interactions?

Coadministration of JARDIANCE with diuretics can result in increased urine volume and frequency of voids, which may enhance the potential for volume depletion.

Coadministration of JARDIANCE with insulin and insulin secretagogues increases the risk of hypoglycemia. A lower dose of insulin or insulin secretagogue may be required to reduce the risk of hypoglycemia when JARDIANCE is used in combination with these agents.

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SELECT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

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 the following pages. Please see Jardiance Prescribing Information and Medication Guide..

How does necrotizing fasciitis of the perineum (Fournier's gangrene) impact patients taking SGLT2 inhibitors?

The JARDIANCE Prescribing Information includes Necrotizing Fasciitis of the Perineum (Fournier's Gangrene) in the Warnings and Precautions section.

Fournier's gangrene is a severe and potentially life-threatening type of necrotizing fasciitis. It is characterized by a mixed infection of both aerobic and anaerobic bacteria and affects the external genitalia, perineum, and perianal region. Fournier's gangrene progresses rapidly and can lead to sepsis, multiple organ failure, and eventually death.[9,10]

In August 2018, the FDA issued a warning about rare cases of Fournier's gangrene in patients with type 2 diabetes taking SGLT2 inhibitors. Rare cases were reported in patients taking dapagliflozin, canagliflozin, and empagliflozin, and the Prescribing Information for each of these products has been updated to include a Warning and Precaution.[10,11]

For more information, please see additional Important Safety Information on page 16 and please see JARDIANCE Prescribing Information.

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SELECT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

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

References: 1. Zinman B, Wanner C, Lachin JM, et al; EMPA-REG OUTCOME Investigators. *N Engl J Med.* 2015;373(22):2117-2128. **2.** Roden M, Weng J, Eilbracht J, et al; EMPA-REG MONO Trial Investigators. *Lancet Diabetes Endocrinol.* 2013;1(3):208-219. **3.** Häring HU, Merker L, Seewaldt-Becker E, et al; EMPA-REG MET Trial Investigators. *Diabetes Care.* 2014;37(6):1650-1659. **4.** 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. Accessed June 12, 2019. **5.** What Are Yeast Infections? Urology Care Foundation. www.urologyhealth.org/ urologic-conditions/yeast-infections. Accessed June 12, 2019. **6.** Häring HU, Merker L, Seewaldt-Becker E, et al; EMPA-REG METSU Trial Investigators. *Diabetes Care.* 2013;36(11):3396-3404. **7.** Rosenstock J, Jelaska A, Zeller C, et al; EMPA-REG BASAL™ Trial Investigators. *Diabetes Obes Metab.* 2015;17(10):936-948. **8.** Kovacs CS, Seshiah V, Swallow R, et al; EMPA-REG PIO™ Trial Investigators. *Diabetes Obes Metab.* 2014;16(2):147-158. **9.** Data on file. Boehringer Ingelheim Pharmaceuticals, Inc. **10.** Bersoff-Matcha SJ, Chamberlain C, Cao C, Kortepeter C, Chong WH. *Ann Intern Med.* [Epub ahead of print May 7, 2019] doi: 10.7326/M19-0085. **11.** US Food and Drug Administration. FDA warns about rare occurrences of a serious infection of the genital area with SGLT2 inhibitors for diabetes. https://www.fda.gov/drugs/drug-safety-and-availability/fda-warns-about-rare-occurrences-serious-infection-genital-area-sglt2-inhibitors-diabetes. Accessed June 12, 2019.

Is there a risk of developing necrotizing fasciitis of the perineum (Fournier's gangrene) in patients treated with JARDIANCE?

The JARDIANCE Prescribing Information includes Necrotizing Fasciitis of the Perineum (Fournier's Gangrene) in the Warnings and Precautions section.

Patient safety is our utmost priority, and we actively monitor the safety of our products on an ongoing basis.[9]

No cases of necrotizing fasciitis of the perineum (Fournier's gangrene) have been reported in the clinical trial program investigating JARDIANCE in patients with type 2 diabetes (N >15,000 patients).[9]

We have received postmarketing case reports of this event, and we are continuing to evaluate the identified cases. We remain confident in the positive benefit-risk profile of JARDIANCE and JARDIANCE-containing products, as outlined in the Prescribing Information.[9]

For more information, please see additional Important Safety Information on page 18 and please see JARDIANCE Prescribing Information.

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FOR ADULTS WITH
ESTABLISHED CV DISEASE AND TYPE 2 DIABETES

More and more cardiologists are prescribing JARDIANCE.9* Are you?

FOR ADDITIONAL INFORMATION, VISIT
JARDIANCEhcp.com

*As measured by NBRx through 1/1/19.

INDICATIONS AND LIMITATIONS OF USE

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IMPORTANT SAFETY INFORMATION

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Please see additional Important Safety Information on the preceding pages. Please see Jardiance Prescribing Information and Medication Guide.

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