JARDIANCE®: A POWERFUL PARTNER

JARDIANCE® is indicated in adult patients with type 2 diabetes mellitus to improve glycemic control, when metformin used alone does not provide adequate glycemic control, in combination with: metformin, metformin and a sulfonylurea, pioglitazone (alone or with metformin), linagliptin and metformin, basal or prandial insulin (alone or with metformin), when the existing therapy, along with diet and exercise, does not provide adequate glycemic control.[1]

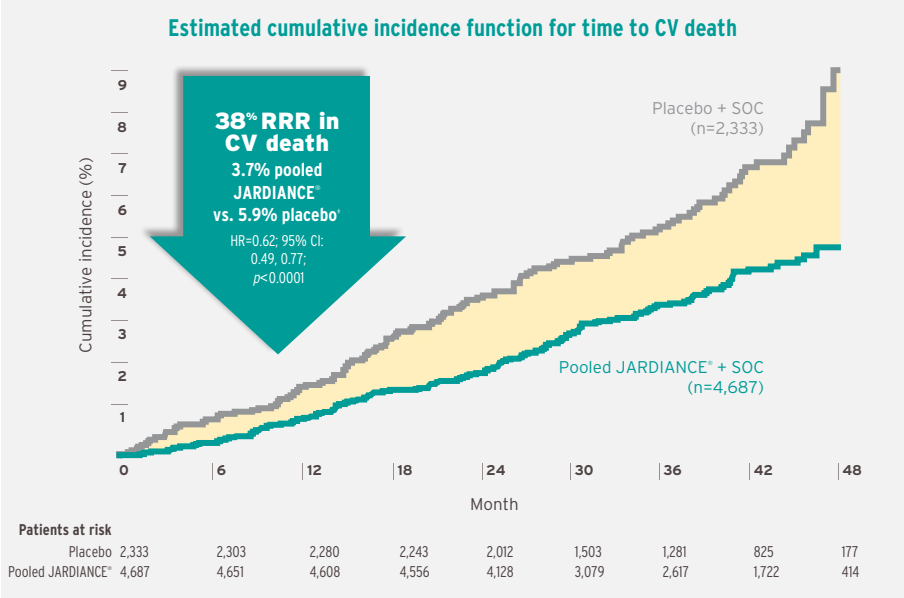
JARDIANCE® is indicated as an adjunct to diet, exercise and standard care therapy to reduce the incidence of cardiovascular death in patients with type 2 diabetes mellitus and established cardiovascular disease.[1]

Jardiance (empagliflozin)

CARDIOVASCULAR CONSIDERATIONS

In patients with T2D and established CV disease

JARDIANCE®, as an adjunct to standard of care therapy*, **reduced the risk of CV death** vs. placebo[1,2†‡] (other adjudicated endpoint)



Adapted from JARDIANCE® Product Monograph and Zinman B, et al.

Demonstrated NNT with JARDIANCE® for 3 years to prevent one CV death

NNT=46

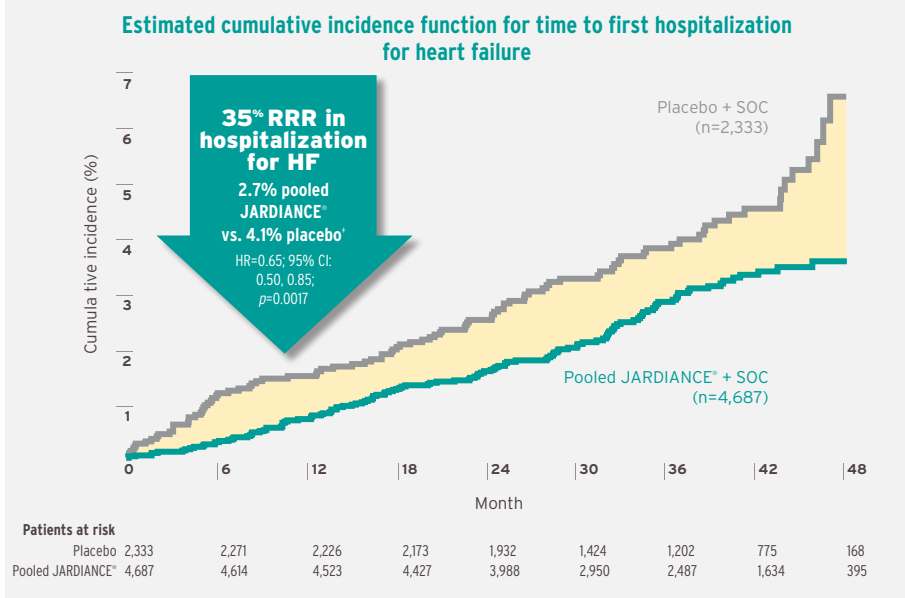
JARDIANCE® demonstrated 14% RRR in the MACE-3 primary analysis vs. placebo (10.5% pooled JARDIANCE® [n=490] vs. 12.1% placebo [n=282]).[1,2‡]
HR=0.86; 95% CI: 0.74, 0.99; *p*=0.0382

There was no significant change in non-fatal MI or non-fatal stroke.[1]

T2D=type 2 diabetes; CV=cardiovascular; SOC=standard of care; RRR=relative risk reduction; HR=hazard ratio; CI=confidence interval; NNT=number needed to treat; MACE-3=Major Adverse Cardiovascular Events; MI=myocardial infarction.
* Baseline therapies included: renin angiotensin system inhibitors (81%), beta-blockers (65%), diuretics (43%), anti-thrombotic therapy (89%), lipid-lowering medication (81%), metformin (74%), insulin (48%), sulfonylurea (43%).
† EMPA-REG OUTCOME study: double-blind, placebo-controlled, event-driven study evaluating empagliflozin 10 mg and 25 mg as add-on to standard of care therapy in reducing CV events in T2D patients with ≥1 of: coronary artery disease, peripheral artery disease, history of MI, history of stroke. Primary endpoint was time to first event in composite endpoint of CV death, non-fatal MI, or non-fatal stroke (Major Adverse Cardiovascular Events [MACE-3]).
‡ Pre-specified pooled analysis of JARDIANCE® 10 and 25 mg vs. placebo in the treated set (patients receiving ≥1 dose of study drug).

In patients with T2D and established CV disease

JARDIANCE®, as an adjunct to standard of care therapy*, **reduced the risk of heart failure requiring hospitalization** vs. placebo[1,2†‡] (other adjudicated endpoint)



Adapted from JARDIANCE® Product Monograph and Zinman B, et al.

Demonstrated NNT with JARDIANCE® for 3 years to prevent one hospitalization for HF

NNT=72

HF=heart failure.
* Baseline therapies included: renin angiotensin system inhibitors (81%), beta-blockers (65%), diuretics (43%), anti-thrombotic therapy (89%), lipid-lowering medication (81%), metformin (74%), insulin (48%), sulfonylurea (43%).
† EMPA-REG OUTCOME study: double-blind, placebo-controlled, event-driven study evaluating empagliflozin 10 mg and 25 mg as add-on to standard of care therapy in reducing CV events in T2D patients with ≥1 of: coronary artery disease, peripheral artery disease, history of MI, history of stroke. Primary endpoint was time to first event in composite endpoint of CV death, non-fatal MI, or non-fatal stroke (Major Adverse Cardiovascular Events [MACE-3]).
‡ Pre-specified pooled analysis of JARDIANCE® 10 and 25 mg vs. placebo in the treated set (patients receiving ≥1 dose of study drug).

A1C CONSIDERATIONS

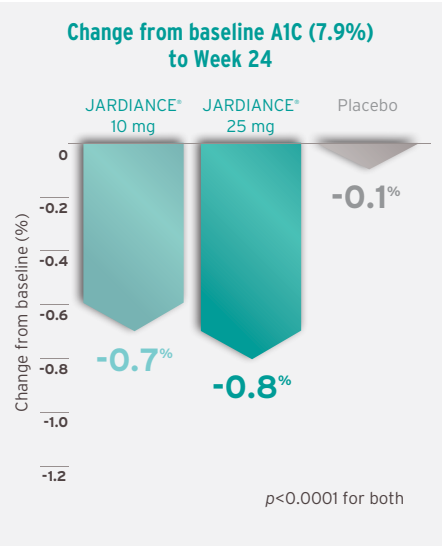
WEIGHT CONSIDERATIONS

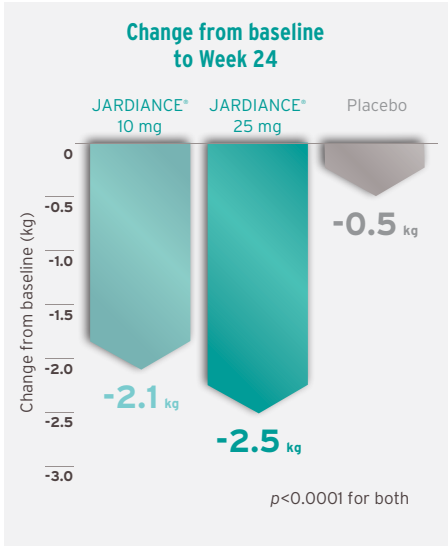
In T2D patients with inadequate glycemic control

JARDIANCE®, as an add-on to metformin, provided...

powerful
A1C reductions
vs. placebo[1,3*]

significant
reductions in body weight
vs. placebo[1,3*] (2º endpoint)



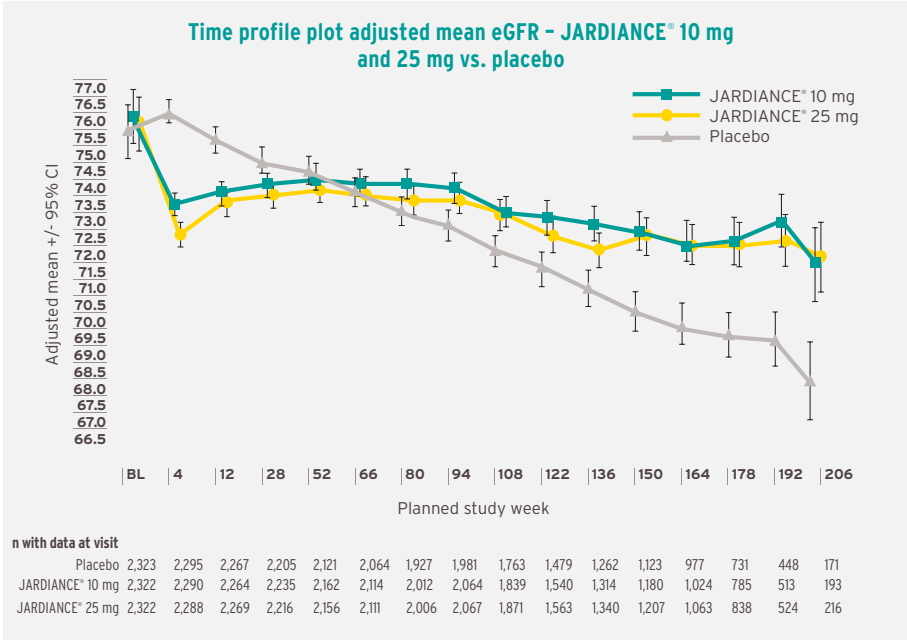


JARDIANCE® is not indicated for weight loss.

A1C=glycated hemoglobin.
* 24-week, double-blind, placebo-controlled study of T2D patients evaluating the efficacy and safety of empagliflozin 10 mg (n=217) and 25 mg (n=213) as add-on to metformin vs. placebo (n=207) plus metformin ≥1500 mg (maximum tolerated dose, or maximum dose from local label). Primary endpoint was A1C reduction at 24 weeks.

RENAL CONSIDERATIONS

In the EMPA-REG CV outcomes trial, mean eGFR for JARDIANCE® groups showed initial decrease, then stabilized, whereas mean eGFR for placebo showed progressive decline.[1]



Adapted from JARDIANCE® Product Monograph.

Increases in serum sodium and serum phosphate above upper limit of normal and decreases in serum potassium and serum bicarbonate below lower limit of normal occurred more frequently in patients receiving JARDIANCE® than those receiving placebo.

In the overall population, increases in serum creatinine and decreases in eGFR:[1]
In a pool of four placebo-controlled trials, mean change from baseline for:
- eGFR (mL/min/1.73 m²) at Week 24 was -0.55, -1.41 and -0.32
- creatinine (µmol/L) was 0.66, 1.28 and 0.35

for JARDIANCE® 10 mg, 25 mg and placebo, respectively.

JARDIANCE® can be used in patients with eGFR 30 mL/min/1.73 m² and above[1]

JARDIANCE® is contraindicated in patients with severe renal impairment (eGFR <30 mL/min/1.73 m²), end-stage renal disease and patients on dialysis. The glucose-lowering benefit of JARDIANCE® decreases with declining renal function.

Assess renal function prior to and regularly during JARDIANCE® treatment. In patients with eGFR <60 mL/min/1.73 m², more intensive monitoring for glycemic and renal biomarkers and signs and symptoms of renal dysfunction is recommended (especially if eGFR <45 mL/min/1.73 m²). Discontinue if eGFR falls below 30 mL/min/1.73 m² during treatment.

There have been post-marketing reports of acute kidney injury, some requiring hospitalization and dialysis, in patients receiving SGLT2 inhibitors.

eGFR=estimated glomerular filtration rate; BL=baseline.

JARDIANCE® offers convenient, once-daily oral dosing

JARDIANCE® DOSING

Recommended starting dose[1]

10 mg OD

Increase to

25 mg OD

In patients tolerating JARDIANCE® 10 mg once daily and requiring additional glycemic control[1]

Tablets shown are not actual size.

With or without food, at any time of the day

Renal impairment
The glucose-lowering efficacy of JARDIANCE® declines with decreasing renal function.
- Contraindicated in patients with severe renal impairment (eGFR <30 mL/min/1.73 m^2), end-stage renal disease or patients on dialysis
- No dosage adjustment necessary in patients with mild to moderate renal impairment
- More intensive monitoring of glycemic and renal biomarkers and signs and symptoms of renal dysfunction in patients with eGFR <60 mL/min/1.73 m^2 (especially if eGFR <45 mL/min/1.73 m^2)
- Discontinue if eGFR falls to a level persistently <30 mL/min/1.73 m^2

Hepatic impairment
- No dosage adjustment needed for patients with mild/moderate hepatic impairment
- Not recommended for use in patients with severe hepatic impairment

General dosing considerations
- Use with caution in patients taking diuretics, particularly loop diuretics
- No dosage adjustment required based on age (however, renal function and risk of volume depletion should be taken into account)
- When JARDIANCE® is added to a sulfonylurea or insulin, a lower dose of the sulfonylurea or insulin may be considered to reduce the risk of hypoglycemia

Please see Product Monograph for complete dosing and administration information.

OD=once daily.

SYNJARDY® contains empagliflozin and metformin in a single tablet[5]

AVAILABLE SYNJARDY® DOSES[5]

2x daily
empagliflozin/metformin

5/500 mg	5/850 mg	5/1000 mg
12.5/500 mg	12.5/850 mg	12.5/1000 mg

Tablets shown are not actual size.

Patients switching from separate tablets of empagliflozin (10 mg or 25 mg total daily dose) and metformin to SYNJARDY® should receive the same daily dose of empagliflozin and metformin already being taken or the nearest therapeutically appropriate dose of metformin.

The maximum recommended daily dose is 25/2000 mg.

With meals, twice daily

The dosage should be individualized on the basis of the patient's current regimen, effectiveness, and tolerability, while not exceeding the recommended daily dose.

SYNJARDY® (empagliflozin and metformin hydrochloride) is indicated as an adjunct to diet and exercise to improve glycemic control in adult patients with type 2 diabetes mellitus inadequately controlled on:
- metformin
- sulfonylurea in combination with metformin
- pioglitazone in combination with metformin
- insulin in combination with metformin

Or in patients already being treated and achieving glycemic control with:
- metformin and empagliflozin as separate tablets
- sulfonylurea in combination with metformin and empagliflozin as separate tablets
- pioglitazone in combination with metformin and empagliflozin as separate tablets
- insulin in combination with metformin and empagliflozin as separate tablets

Please refer to the Product Monograph at www.SynjardyPM.ca for contraindications, warnings, precautions, adverse reactions, interactions, dosing and conditions of clinical use. The Product Monograph is also available by calling 1-800-263-5103 ext. 84633.

Synjardy® (empagliflozin/metformin HCl)

Jardiance®
(empagliflozin)

The #1 dispensed SGLT2i in Canada[4]*

Indications and clinical use not discussed elsewhere in the piece

Monotherapy: JARDIANCE® (empagliflozin) is indicated for use as an adjunct to diet and exercise to improve glycemic control in adult patients with type 2 diabetes mellitus for whom metformin is inappropriate due to contraindications or intolerance.

Important limitation of use: Use of JARDIANCE® with insulin mix (regular or analogue mix) has not been studied. Therefore, JARDIANCE® should not be used with insulin mix.

Contraindications

- Patients with severe renal impairment (eGFR <30 mL/min/1.73 m^2), end-stage renal disease and patients on dialysis

Most serious warnings and precautions

Diabetic ketoacidosis (DKA): Cases of DKA, a serious, life-threatening condition requiring urgent hospitalization, have been reported for JARDIANCE® or other SGLT2i, including fatal cases for patients taking JARDIANCE® and atypical cases with blood glucose <13.9 mmol/L (250 mg/dL). Consider the risk of DKA if non-specific symptoms occur, regardless of blood glucose level, and **immediately discontinue JARDIANCE® and assess for DKA**. JARDIANCE® should not be used for the treatment of DKA or in patients with a history of DKA. JARDIANCE® is not indicated, and should not be used, in patients with type 1 diabetes.

Other relevant warnings and precautions

- Not recommended in volume-depleted patients; drops in blood pressure; monitor volume status and electrolytes
- Caution in patients at high risk for cerebrovascular accidents
- Temporarily discontinue in situations predisposing to ketoacidosis
- Caution when reducing concomitant insulin dose
- Hypoglycemia when used in combination with insulin secretagogues or insulin
- Risk and monitoring of LDL-C increases
- Genital mycotic infections
- Urinary tract infections
- Necrotizing fasciitis of the perineum (Fournier's gangrene)
- Caution in patients with elevated hematocrit
- Not recommended in patients with severe hepatic impairment
- Serious hypersensitivity reactions
- Intravascular volume contraction, increases in serum creatinine, decreases eGFR; assess renal function prior to initiation and regularly thereafter; monitor renal function with concomitant drug use; more intensive monitoring if eGFR <60 mL/min/1.73 m^2 (especially if eGFR <45 mL/min/1.73 m^2); discontinue if eGFR <30 mL/min/1.73 m^2
- Acute kidney injury
- Use in settings of reduced oral intake or fluid loss
- Do not use during pregnancy or breastfeeding
- Do not use in patients <18 years; caution in patients ≥65 years and ≥75 years; not recommended in patients ≥85 years
- Patients will test positive for glucose in urine

For more information

Please refer to the Product Monograph at www.JardiancePM.ca for important information relating to adverse events, drug interactions, dosing, and conditions of clinical use. The Product Monograph is also available by calling 1-800-263-5103 ext. 84633.

eGFR=estimated glomerular filtration rate; SGLT2i=sodium-glucose co-transporter 2 inhibitor; LDL-C=low-density lipoprotein cholesterol.
* Comparative clinical significance not established.

References: 1. JARDIANCE® Product Monograph, Boehringer Ingelheim (Canada) Ltd., April 15, 2020. **2.** Zinman B, et al. Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes. *N Engl J Med* 2015;373(22):2117–28. **3.** Häring HU, et al. Empagliflozin as Add-On to Metformin in Patients with Type 2 Diabetes: A 24-Week, Randomized, Double-Blind, Placebo-Controlled Trial. *Diabetes Care* 2014;37(6):1650–9. **4.** IQVIA TRx Data, February 12, 2020. **5.** SYNJARDY® Product Monograph, Boehringer Ingelheim (Canada) Ltd., April 28, 2020.

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EMP-CA-101071
EMP-LI-101071

Boehringer Ingelheim

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