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.

Add-on combination: JARDIANCE® is indicated in adult patients with type 2 diabetes mellitus to improve glycemic control, when metformin 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.

Add-on combination in patients with established cardiovascular disease: 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.

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.

SGLT2i = sodium-glucose co-transporter 2 inhibitor.
*Comparative clinical significance not established.

The #1 dispensed SGLT2i in Canada.[1*]

Jardiance® (empagliflozin)

Contraindications:
- Patients with severe renal impairment (eGFR <30 mL/min), end-stage renal disease and patients on dialysis

Most Serious Warning and Precaution:
Diabetic Ketoacidosis (DKA): Cases of DKA, a serious, life-threatening condition requiring urgent hospitalization, have been reported for JARDIANCE® and other SGLT2i, including fatal cases and atypical cases with blood glucose <13.9 mmol/L (250 mg/dL). Assess for DKA immediately if non-specific symptoms occur, regardless of blood glucose level, and **discontinue JARDIANCE® immediately**. 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 during treatment; monitor renal function with concomitant drug use; more intensive monitoring if eGFR <60 mL/min (especially if eGFR <45 mL/min); discontinue if eGFR <30 mL/min
- 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:
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.

References: 1. IQVIA TRx Data, March 2019. 2. JARDIANCE Product Monograph. Boehringer Ingelheim, April 11, 2019. 3. Zinman B, *et al*. Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes. *N Engl J Med*. 2015;373(22):2117-28. 4. 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.

Jardiance® (empagliflozin)

EMP-CA-100649
EMP-LI-100649

Boehringer Ingelheim

Lilly

AIC CONSIDERATIONS

WEIGHT CONSIDERATIONS

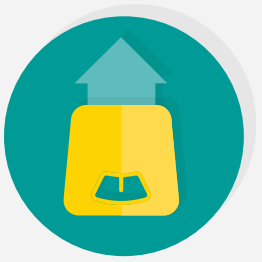
In T2D patients with inadequate glycemic control

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

powerful AIC reductions vs. placebo[2,4§]

Change from baseline AIC (7.9%) to week 24:
-0.7% JARDIANCE® 10 mg, -0.8% JARDIANCE® 25 mg, -0.1 placebo ($p<0.0001$ for both)

significant reductions in body weight vs. placebo (secondary endpoint)[2,4§]



Change from baseline to week 24:
-2.1 kg JARDIANCE® 10 mg, -2.5 kg JARDIANCE® 25 mg, -0.5 kg placebo ($p<0.0001$ for both)

JARDIANCE® is not indicated for weight loss.

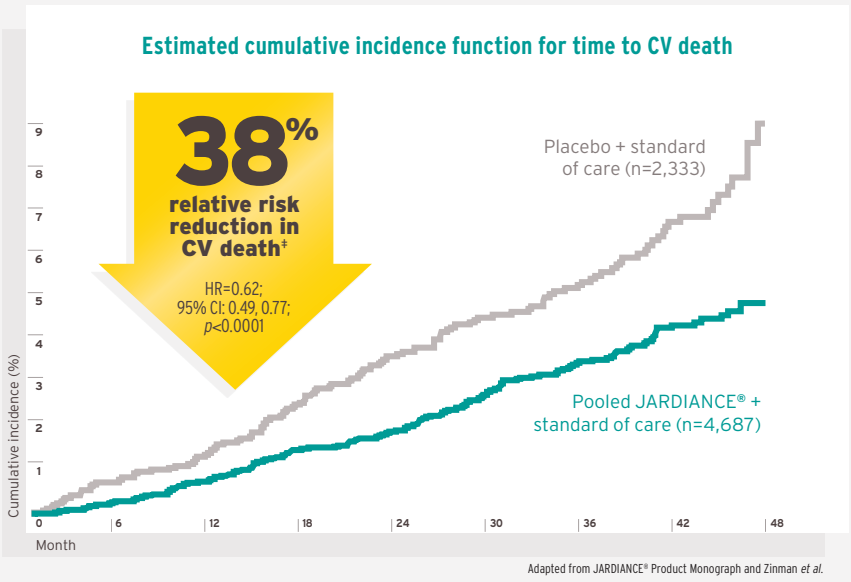
T2D = type 2 diabetes.

§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.

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. (other adjudicated endpoint)[2,3†‡]



Adapted from JARDIANCE® Product Monograph and Zinman *et al.*

Patients at risk									
Placebo	2,333	2,303	2,280	2,243	2,012	1,503	1,281	825	177
Pooled JARDIANCE®	4,687	4,651	4,608	4,556	4,128	3,079	2,617	1,722	414

Absolute risk for CV death:
5.9% placebo vs. 3.7% pooled JARDIANCE®

NNT=46

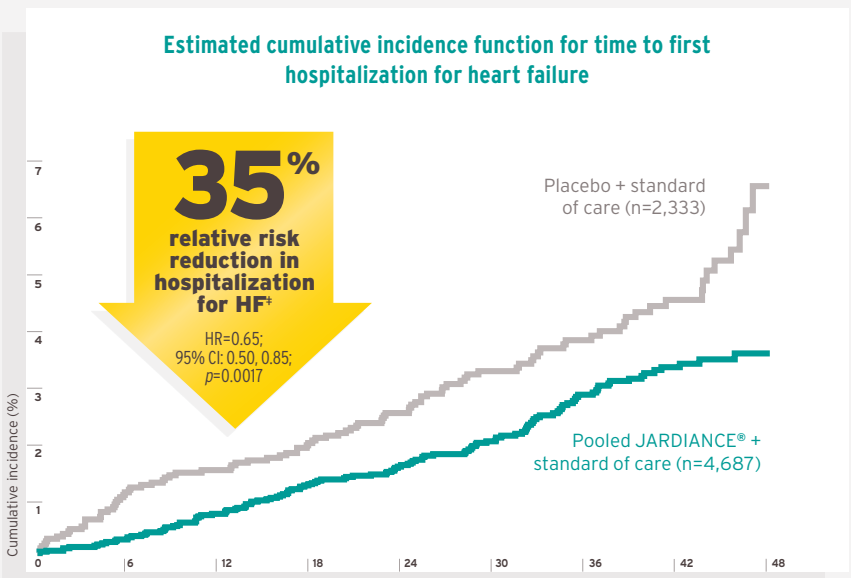
JARDIANCE® demonstrated 14% relative risk reduction in the MACE-3 primary analysis vs. placebo.‡

Patients with event: 490 (10.5%) pooled JARDIANCE® vs. 282 (12.1%) placebo; 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.

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. (other adjudicated endpoint)[2,3†‡]



Adapted from JARDIANCE® Product Monograph and Zinman *et al.*

Patients at risk									
Placebo	2,333	2,271	2,226	2,173	1,932	1,424	1,202	775	168
Pooled JARDIANCE®	4,687	4,614	4,523	4,427	3,988	2,950	2,487	1,634	395

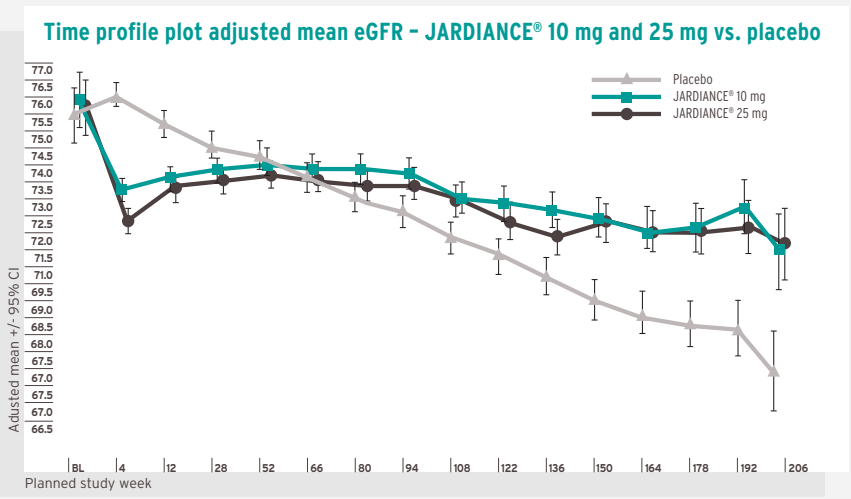
Absolute risk for hospitalization for HF:
4.1% placebo vs. 2.7% pooled JARDIANCE®

NNT=72

CV = cardiovascular; eGFR = estimated glomerular filtration rate; HF = heart failure; MI = myocardial infarction; NNT = number needed to treat; T2D = type 2 diabetes.
*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).

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.[2]



Adapted from JARDIANCE® Product Monograph.

n with data at visit																
Placebo	2,323	2,295	2,267	2,205	2,121	2,064	1,927	1,981	1,763	1,479	1,262	1,123	977	731	448	171
JARDIANCE® 10 mg	2,322	2,290	2,264	2,235	2,162	2,114	2,012	2,064	1,839	1,540	1,314	1,180	1,024	785	513	193
JARDIANCE® 25 mg	2,322	2,288	2,269	2,216	2,156	2,111	2,006	2,067	1,871	1,563	1,340	1,207	1,063	838	524	216

In the overall population, increases in serum creatinine and decreases in eGFR:
In a pool of four placebo-controlled trials, mean change from baseline for:
- eGFR (mL/min/1.73 m^2) 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 and above.[2]

JARDIANCE® is contraindicated in patients with severe renal impairment (eGFR <30 mL/min/1.73 m^2), 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, more intensive monitoring for glycemic and renal biomarkers and signs and symptoms of renal dysfunction is recommended (especially if eGFR <45 mL/min). Discontinue if eGFR falls below 30 mL/min during treatment.