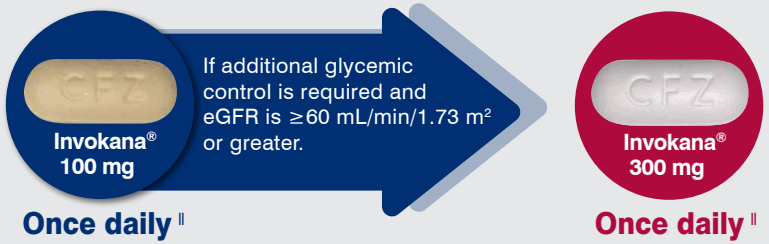
SIMPLE
DOSING REGIMEN

The recommended starting dose of **Invokana®** is 100 mg once daily, and the dose can be increased to 300 mg once daily in patients who require additional glycemic control [4].



Once daily ‖ **Once daily** ‖

(Should be initiated in patients with an eGFR higher than 45 mL/min/1.73m²)

* To characterize single- and multiple-dose pharmacokinetics of Invokana® and its O-glucuronide metabolites (M5 and M7) and pharmacodynamics of Invokana® in T2DM patients, 36 patients were randomized to receive Invokana® 50, 100, or 300 mg/day or placebo for 7 days [2].

† In this 52-week, randomized, double-blind, active-controlled, phase 3 study, 755 patients whose T2DM were inadequately controlled (HbA1c ≥7.0% and ≤10.5%) with metformin plus sulfonylurea received Invokana® 300 mg or sitagliptin 100 mg daily[6].

‡ Using integrated claims and lab data from a US health plan of commercial and Medicare Advantage enrollees, this matched-control cohort study assessed adult T2DM patients receiving treatment with Invokana® or DPP-4 inhibitors (1 April 2013–31 December 2013). Cohorts were chosen hierarchically; the first pharmacy claim for Invokana® was identified as the index date; then the first pharmacy claim for a DPP-4 inhibitor was identified and index date set. Eligible patients had 6 months of continuous health plan enrollment before the index date (baseline) and 9 months after (follow-up) and no evidence of index drug in baseline. Patients were matched 1:1 using propensity score matching. The matched Invokana® and DPP-4 inhibitor cohorts (53.2% treated with sitagliptin) included 2,766 patients each. Changes in HbA1c and percentages of patients with HbA1c <8% and <7% during the follow-up were evaluated[7].

§ In this randomized, double-blind, four-arm, parallel-group, phase 3 study, 1,284 patients whose T2DM were inadequately controlled (HbA1c ≥7.0% and ≤10.5%) with metformin monotherapy received Invokana® 100 mg or 300 mg, sitagliptin 100 mg, or placebo for a 26 week, placebo- and active-controlled period followed by a 26 week, active-controlled period (placebo group switched to sitagliptin [placebo/sitagliptin])[8].

‖ Recommended to be taken before the first meal of the day and should not be initiated in patients with an eGFR less than 45 mL/min/1.73 m².

DPP-4 = dipeptidyl peptidase-4. eGFR = estimated glomerular filtration rate.

References
1. Plosker GL. Canagliflozin: a review of its use in patients with type 2 diabetes mellitus. Drugs 2014;74:807-824. 2. Devineni D, Curtin CR, Polidori D, et al. Pharmacokinetics and pharmacodynamics of canagliflozin, a sodium glucose co-transporter 2 inhibitor, in subjects with type 2 diabetes mellitus. J Clin Pharmacol 2013;53:601-610. 3. Scheen AJ. Pharmacodynamics, efficacy and safety of sodium-glucose co-transporter type 2 (SGLT2) inhibitors for the treatment of type 2 diabetes mellitus. Drugs 2015;75:33-59. 4. Invokana® prescribing information (effective date: 20 Nov 2019). 5. Polidori D, Sha S, Mudaliar S, et al. Canagliflozin lowers postprandial glucose and insulin by delaying intestinal glucose absorption in addition to increasing urinary glucose excretion: results of a randomized, placebo-controlled study. Diabetes Care 2013;36:2154-2161. 6. Schernthaner G, Gross JL, Rosenstock J, et al. Canagliflozin compared with sitagliptin for patients with type 2 diabetes who do not have adequate glycemic control with metformin plus sulfonylurea: a 52-week randomized trial. Diabetes Care 2013;36:2508-2515. 7. Thayer S, Chow W, Korrer S, Aguilar R. Real-world evaluation of glycemic control among patients with type 2 diabetes mellitus treated with canagliflozin versus dipeptidyl peptidase-4 inhibitors. Curr Med Res Opin 2016;32:1087-1096. 8. Lavalle-González FJ, Januszewicz A, Davidson J, et al. Efficacy and safety of canagliflozin compared with placebo and sitagliptin in patients with type 2 diabetes on background metformin monotherapy: a randomised trial. Diabetologia. 2013;56:2582-2592. 9. Sha S, Devineni D, Ghosh A, et al. Pharmacodynamic effects of canagliflozin, a sodium glucose co-transporter 2 inhibitor, from a randomized study in patients with type 2 diabetes. PLoS One 2014;9:e105638.

INVOKANA® tablets 100 mg, 300 mg
ABBREVIATED PRESCRIBING INFORMATION
ACTIVE INGREDIENT(S): canagliflozin. **INDICATION(S):** INVOKANA is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. INVOKANA is also indicated to reduce the risk of major adverse cardiovascular events (cardiovascular death, nonfatal myocardial infarction and nonfatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease (CVD).INVOKANA is not recommended in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. **DOSAGE & ADMINISTRATION:** Assessment of renal function is recommended prior to initiation of INVOKANA and periodically thereafter. In patients with volume depletion not previously treated with canagliflozin, normalize volume status before initiating INVOKANA. Recommended starting dose is 100 mg once daily, taken before the first meal of the day. In patients tolerating INVOKANA 100 mg once daily who have an eGFR of 60 mL/min/1.73 m2 or greater and require additional glycemic control, the dose can be increased to 300 mg once daily. The dose of INVOKANA is limited to 100 mg once daily in patients with moderate renal impairment with an eGFR of 45 to less than 60 mL/min/1.73 m². Initiation is not recommended in patients with an eGFR less than 45 mL/min/1.73 m2. Use is not recommended when eGFR is persistently less than 45 mL/min/1.73 m². **CONTRAINDICATIONS:** Serious hypersensitivity reaction to INVOKANA, such as anaphylaxis or angioedema. Severe renal impairment (eGFR less than 30 mL/min/1.73 m²), end stage renal disease or patients on dialysis. **SPECIAL WARNINGS & PRECAUTIONS:** Lower Limb Amputation: An approximately 2-fold increased risk of lower limb amputations associated with INVOKANA use was observed in patients with type 2 diabetes who had established cardiovascular disease (CVD) or were at risk for CVD. Consider factors that may increase risk of amputation before initiating. Monitor patients for infection, new pain or tenderness, sores or ulcers involving lower limbs, and discontinue if these complications occur. Hypotension: Causes intravascular volume contraction. Before initiating INVOKANA, assess and correct volume status in patients with renal impairment (eGFR less than 60 mL/min/1.73 m²), the elderly, patients with low systolic blood pressure, or patient on either diuretics or medications that interfere with the renin-angiotensin-aldosterone system. Monitor for signs and symptoms during therapy. Ketoacidosis: Fatal cases of ketoacidosis have been reported in INVOKANA patients. Assess for ketoacidosis in patients who present with signs and symptoms consistent with severe metabolic acidosis. Discontinue INVOKANA if ketoacidosis is suspected, and prompt treatment should be instituted. Consider factors in patient history that may predispose to ketoacidosis before initiating INVOKANA. Acute Kidney Injury: INVOKANA causes intravascular volume contraction and can cause acute kidney injury. Consider factors that may predispose patients to acute kidney injury before initiating INVOKANA. Monitor patients for signs and symptoms of acute kidney injury. Discontinue INVOKANA promptly and institute treatment if acute kidney injury occurs. Dosage adjustment and more frequent renal function monitoring are recommended in patients with an eGFR below 60 mL/min/1.73 m2. Urosepsis and Pyelonephritis: Evaluate patients for signs and symptoms of urinary tract infections and treat promptly, if indicated. Hypoglycemia: A lower dose of insulin or insulin secretagogue may be required to minimize the risk of hypoglycemia when used in combination with INVOKANA. Necrotizing Fasciitis of the Perineum (Fournier's Gangrene): Assess patients for necrotizing fasciitis if patient treated with INVOKANA presenting with pain or tenderness, erythema, or swelling in the genital or perineal area, along with fever or malaise. If suspected, start treatment immediately with broad-spectrum antibiotics and, if necessary, surgical debridement. Discontinue INVOKANA, closely monitor blood glucose levels, and provide appropriate alternative therapy for glycemic control. Genital Mycotic Infections: Monitor and treat appropriately. Hypersensitivity Reactions: Discontinue INVOKANA; treat per standard of care and monitor until signs and symptoms resolve. Bone Fracture: Consider factors that contribute to fracture risk prior to initiating INVOKANA. Increases in Low-Density Lipoprotein (LDL-C): Monitor LDL-C and treat per standard of care. **SIDE EFFECTS:** Female genital mycotic infections, urinary tract infections, increased urination, male genital mycotic infections, vulvovaginal pruritus, thirst, constipation and nausea. Lower limb amputation. Refer to full prescribing information for other side effects. **PREGNANCY & LACTATION:** INVOKANA is not recommended during the second and third trimesters of pregnancy. Use of INVOKANA is not recommended while breastfeeding. **INTERACTIONS:** UDP-Glucuronosyl Transferase (UGT) Enzyme Inducers. Digoxin.
PLEASE REFER TO FULL PRESCRIBING INFORMATION BEFORE PRESCRIBING.
aPI version to be quoted on promotional material: Invokana aPI ver 4.0

CP-248935 Aug2021

Manufactured by: Janssen Pharmaceutical Companies of Johnson & Johnson

Distributed by: DCH AURIGA

DCH Auriga (Hong Kong) Limited
11/F Wyler Centre 1, 202-210 Tai Lin Pai Road,
Kwai Chung, Hong Kong
Tel: 3619 2823

Invokana® canagliflozin tablets

Fight against Diabetes with
A Potent SGLT2 Inhibitor

Invokana® canagliflozin tablets

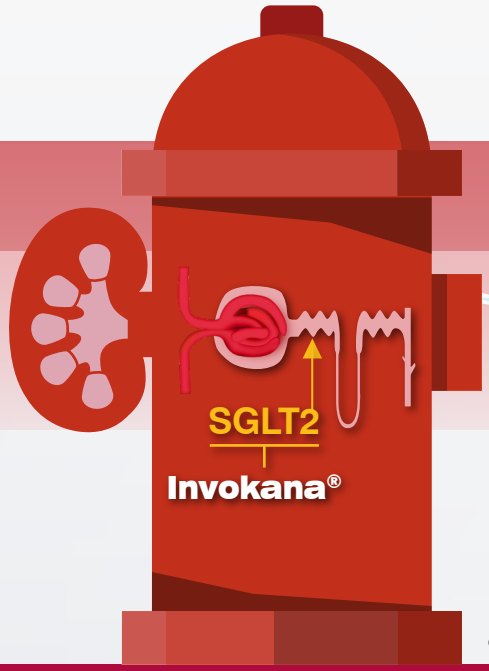
24hr **Glycemic Control** via Induced Therapeutic Glucosuria[1]

Manufactured by: Janssen Pharmaceutical Companies of Johnson & Johnson

Distributed by: DCH AURIGA

Invokana® canagliflozin tablets

Invokana® (canagliflozin): Reduced renal threshold for glucose (RT_G) to remove excess glucose



Invokana®, a selective inhibitor of SGLT2, **REDUCES** blood glucose levels by **LOWERING** RT_G and **INCREASING** urinary glucose excretion (UGE)[1].

24-h mean RT_G *,2 | **Invokana®: 4.3-4.7 mmol/L**

By **DECREASING** RT_G, SGLT2 inhibitors **INCREASE** **UGE** in T2DM patients[3].

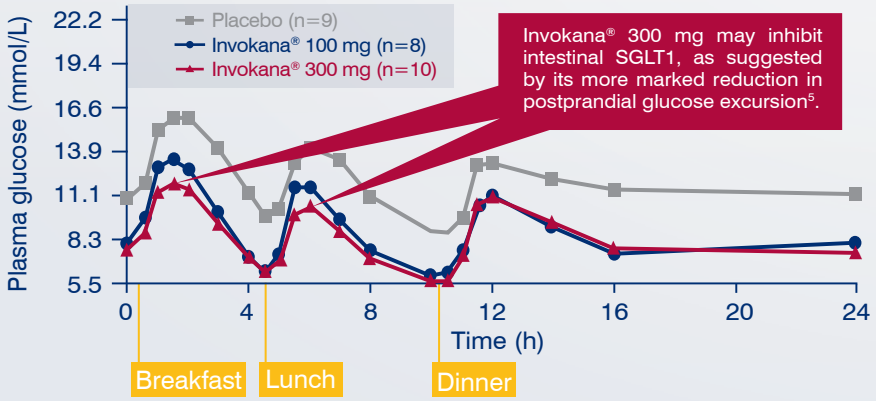
Invokana® ~100 g

UGE per day [4]

Graphics of sugar cubes shown does not proportionally represent the actual amount of glucose excreted.

Invokana®: All-day effectiveness against hyperglycemia

Mean plasma glucose concentration-time profiles at day 7 *,2



Invokana® 300 mg may inhibit intestinal SGLT1, as suggested by its more marked reduction in postprandial glucose excursion[5].

DIFFERENCE IN LS MEAN CHANGE

VS

PLACEBO

Invokana® 100 mg: -2.7 mmol/L

Invokana® 300 mg: -3.2 mmol/L

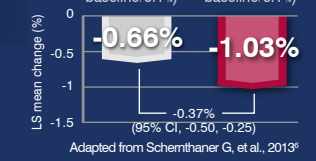
CI = confidence interval. LS = least squares. PPG = postprandial glucose. RT_G = renal threshold for glucose. SGLT1 = sodium-glucose cotransporter 1. SGLT2 = sodium-glucose cotransporter 2. T2DM = type 2 diabetes mellitus. UGE = urinary glucose excretion.

Improved glycemic control

A1C

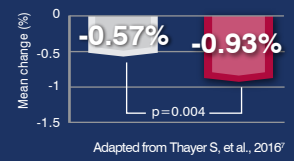
Superior reductions in HbA_{1c}

Clinical data†, 6:



Adapted from Schernthaner G, et al., 2013[6]

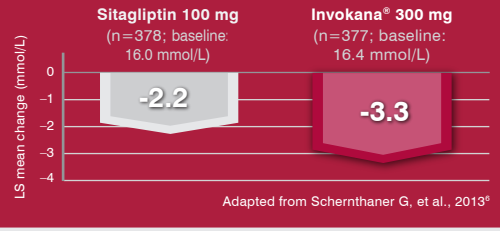
Real-world data‡, 7:



Adapted from Thayer S, et al., 2016[7]

Unique effect on intestinal SGLT1

2-h PPG†, 6



Adapted from Schernthaner G, et al., 2013[6]

Low incidence of hypoglycemia

Documented hypoglycemia§, 8

Since maximum mean reductions in 24-h RT_G is **ABOVE** the typical threshold for hypoglycemia (3.9 mmol/L), Invokana® is **NOT** expected to be associated with an increased risk for hypoglycemia[2, 9].