INVOKANA® (canagliflozin) 100 mg & 300 mg film-coated tablets.

PRESCRIBING INFORMATION
UNITED KINGDOM

Please refer to the Summary of Product Characteristics (SmPC) before prescribing.

INDICATIONS: The treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise as monotherapy when metformin is considered inappropriate due to intolerance or contraindications, or in addition to other medicinal products for the treatment of diabetes.

DOSAGE & ADMINISTRATION: Adults: recommended starting dose: 100 mg once daily. In patients tolerating this dose and with eGFR ≥ 60 mL/min/1.73 m^2 needing tighter glycaemic control, dose can be increased to 300 mg once daily. For oral use, swallow whole. Caution increasing dose in patients ≥ 75 years old, with known cardiovascular disease or for whom initial canagliflozin-induced diuresis is a risk. Correct volume depletion prior to initiation. When add-on, consider lower dose of insulin or insulin secretagogue to reduce risk of hypoglycaemia. **Children:** no data available. **Elderly:** consider renal function and risk of volume depletion. **Renal impairment:** for the treatment of diabetic kidney disease (DKD) as add on to standard of care (SOC) (ACE inhibitors or ARBs), initiate with 100 mg dose. The glycaemic lowering efficacy of canagliflozin is reduced in patients with moderate renal impairment and likely absent in severe renal impairment. If eGFR falls below 60 mL/min/1.73 m^2 during treatment, adjust or maintain dose at 100 mg once daily.

eGFR (mL/min/1.73m^2) or CrCl (mL/min)	**Total daily dose of canagliflozin**
≥ 60	Initiate with 100 mg If tolerating 100 mg and needing additional glycaemic control, increase dose to 300 mg
45 to < 60[a]	Initiate with 100 mg If already taking ***Invokana*** – continue 100 mg
30 to < 45[a, b]	Initiate with 100 mg If already taking ***Invokana*** – continue 100 mg
< 30[a, b]	Do not initiate If already taking ***Invokana*** – continue 100 mg[c]

[a] Consider addition of other anti-hyperglycaemic agents if further glycaemic control is needed
[b] With urinary albumin/creatinine ratio > 300 mg/g [c] Continue until dialysis or renal transplantation
Hepatic impairment: mild or moderate; no dose adjustment. Severe; not studied, not recommended.

CONTRAINDICATIONS: Hypersensitivity to active substance or any excipient.

SPECIAL WARNINGS & PRECAUTIONS: Not for use in type 1 diabetes. **Renal impairment:** regardless of pretreatment, patients on canagliflozin had an initial fall in eGFR that attenuated over time. eGFR < 60 mL/min/1.73 m^2: higher incidence of adverse reactions associated with volume depletion particularly with 300 mg dose; more events of elevated potassium; greater increases in serum creatinine and blood urea nitrogen (BUN); limit dose to 100 mg once daily. Not studied in severe renal impairment. Monitor renal function prior to initiation and at least annually. **Volume depletion:** caution in patients for whom a canagliflozin-induced drop in blood pressure is a risk (e.g. known cardiovascular disease, eGFR < 60 mL/min/1.73 m^2, anti-hypertensive therapy with history of hypotension, on diuretics or elderly). Not recommended with loop diuretics or in volume depleted patients. Monitor volume status and serum electrolytes. **Diabetic ketoacidosis (DKA):** rare DKA cases reported, including life-threatening and fatal. Presentation may be atypical (blood glucose <14mmol/L). Risk appears higher in patients with

moderate to severe decrease in renal function who require insulin. Consider DKA in event of non-specific symptoms. If DKA is suspected or diagnosed, discontinue ***Invokana*** treatment immediately. Interrupt treatment in patients who are undergoing major surgical procedures or have acute serious medical illnesses. Monitoring of (preferably blood) ketone levels is recommended in these patients. Consider risk factors for development of DKA before initiating ***Invokana*** treatment**. Elevated haematocrit:** careful monitoring if already elevated. **Genital mycotic infections:** risk in male and female patients, particularly in those with a history of GMI. **Lower limb amputation:** consider risk factors before initiating. Monitor patients with a higher risk of amputation events, counsel on routine preventative foot care and adequate hydration. Consider discontinuing ***Invokana*** when events preceding amputation occur (e.g. lower-extremity skin ulcer, infection, osteomyelitis or gangrene). **Necrotising fasciitis of the perineum (Fournier's gangrene):** post-marketing cases reported with SGLT2 inhibitors. Rare but serious, patients should seek medical attention if experiencing symptoms including pain, tenderness, erythema, genital/perineal swelling, fever, malaise. If Fournier's gangrene suspected, ***Invokana*** should be discontinued, and prompt treatment instituted. **Urine laboratory assessment:** glucose in urine due to mechanism of action. **Lactose intolerance:** do not use in patients with galactose intolerance, total lactase deficiency or glucose-galactose malabsorption. **Sodium:** essentially "sodium-free".

INTERACTIONS: Diuretics: may increase risk of dehydration and hypotension. **Insulin and insulin secretagogues:** risk of hypoglycaemia; consider lower dose of insulin or insulin secretagogue. **Effects of other medicines on *Invokana*:** enzyme inducers (e.g. St. John's wort, rifampicin, barbiturates, phenytoin, carbamazepine, ritonavir, efavirenz) may decrease exposure of canagliflozin; monitor glycaemic control. Consider dose increase to 300 mg if administered with UGT enzyme inducer. Cholestyramine may reduce canagliflozin exposure; take canagliflozin at least 1 hour before or 4-6 hours after a bile acid sequestrant. **Effects of *Invokana* on other medicines:** monitor patients on digoxin, other cardiac glycosides, dabigatran. Inhibition of Breast Cancer Resistance Protein cannot be excluded; possible increased exposure of drugs transported by BCRP (e.g. rosuvastatin and some anti-cancer agents).

PREGNANCY: No human data. Not recommended.

LACTATION: Unknown if excreted in human milk. Should not be used during breast-feeding.

SIDE EFFECTS: Very common (≥1/10): vulvovaginal candidiasis, hypoglycaemia in combination with insulin or sulphonylurea. **Common (≥1/100 to<1/10):** balanitis or balanoposthitis, urinary tract infection (including pyelonephritis and urosepsis), constipation, thirst, nausea, polyuria or pollakiuria, dyslipidemia, haematocrit increased. **Uncommon (<1/100) but potentially serious:** necrotising fasciitis of the perineum (Fournier's gangrene) (frequency not known), anaphylactic reaction, diabetic ketoacidosis, syncope, hypotension, orthostatic hypotension, urticaria, angioedema, bone fracture, renal failure (mainly in the context of volume depletion), lower limb amputations (mainly of the toe and midfoot). **Refer to SmPC for details and other side effects.**

LEGAL CATEGORY: POM.

PACK SIZES, MARKETING AUTHORISATION NUMBER(S) & BASIC NHS COSTS *Invokana* 100 mg film coated tablets: 30 tablets; EU/1/13/884/002; £39.20. ***Invokana* 300 mg film coated tablets**: 30 tablets; EU/1/13/884/006; £39.20.

MARKETING AUTHORISATION HOLDER: Janssen-Cilag International NV, Turnhoutseweg 30, B-2340 Beerse, Belgium**.**

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard . Adverse events should also be reported to Napp Pharmaceuticals at drugsafetyuk@napp.co.uk.

FURTHER INFORMATION IS AVAILABLE FROM: Napp Pharmaceuticals Ltd. Cambridge Science Park Milton Road, Cambridge, CB4 0AB, UK. For medical information enquiries, please contact medicalinformationuk@napp.co.uk.

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