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

PRESCRIBING INFORMATION:
Please refer to Summary of Product Characteristics (SmPC) before prescribing.

INDICATIONS: In adults with type 2 diabetes mellitus to improve glycaemic control as: monotherapy when diet and exercise alone do not provide adequate glycaemic control and use of metformin considered inappropriate; add-on therapy with other glucose-lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control.

DOSAGE & ADMINISTRATION: Adults: recommended starting dose: 100 mg once daily. In patients tolerating this dose and with eGFR ≥ 60 mL/min/1.73 m2 needing tighter glycaemic control, dose can be increased to 300 mg once daily. 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:** not to be initiated with eGFR < 60 mL/min/1.73 m2. If eGFR falls below this value during treatment, adjust or maintain dose at 100 mg once daily. Discontinue if eGFR persistently < 45 mL/min/1.73 m2. Not for use in end stage renal disease or patients on dialysis. **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. Not to be used for treatment of diabetic ketoacidosis. **Renal impairment:** eGFR < 60 mL/min/1.73 m2: 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 and discontinue when eGFR < 45 mL/min/1.73 m2. 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 (eg, known cardiovascular disease, eGFR < 60 mL/min/1.73 m2, 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. **Elevated haematocrit:** caution. **Genital mycotic infections:** risk in male and female patients, particularly in those with a history of GMI. **Lower limb amputation:** monitor patients with or at high risk of cardiovascular disease. Counsel on routine preventative foot care and adequate hydration. Consider discontinuing Invokana when events preceding amputation occur (eg, lower-extremity skin ulcer, infection, osteomyelitis or gangrene). **Urine laboratory assessment:** glucose in urine due to mechanism of action. **Lactose intolerance:** do not use in patients with galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption. **Diabetic ketoacidosis (DKA):** rare DKA cases reported, including life-threatening and atypical presentation cases. Where 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. Consider risk factors for development of DKA before initiating Invokana treatment.

SIDE EFFECTS: Very common: hypoglycaemia in combination with insulin or sulphonylurea, vulvovaginal candidiasis. **Common:** constipation, thirst, nausea, polyuria or pollakiuria, urinary tract infection (including pyelonephritis and urosepsis), balanitis or balanoposthitis, dyslipidemia, haematocrit increased. **Uncommon (<1/100) but potentially serious:** 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). **Refer to SmPC for other side effects.**

PREGNANCY: No human data. Not recommended.

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

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 (eg, 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 (eg, rosuvastatin and some anti-cancer agents).

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. ® INVOKANA is a registered trade mark of Janssen-Cilag International NV and is used under licence.

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 Janssen-Cilag Ltd on 01494567447 or at dsafety@its.jnj.com.

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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References: 1. Data on File: Canagliflozin_06SEP14_MI_HW_002_VS. The number of patients treated with canagliflozin in the US. **2.** Schernthaner G et al. Diabetes Care 2013; 36(9): 2508-2515. **3.** Stenlöf K et al. Diabetes Obes Metab 2013; 15(4): 372-382. **4.** Forst T et al. Diabetes Obes Metab 2014; 16: 467-477. **5.** Wilding JP et al. Int J Clin Pract 2013; 67 (12): 1267-1282. **6.** Evans M et al. Poster presented at ISPOR 2016. October 29th-November 2nd. Vienna, Austria.