Prescribing Information (Ireland) JARDIANCE® (empagliflozin)

Film-coated tablets containing 10 mg or 25 mg empagliflozin. **Indication:** Jardiance is indicated for 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; in addition to other medicinal products for the treatment of diabetes. For study results with respect to combinations, effects on glycaemic control and cardiovascular events, and the populations studied, refer to the Summary of Product Characteristics. **Dose and Administration:** The recommended starting dose is 10 mg once daily. In patients tolerating empagliflozin 10 mg once daily who have eGFR ≥ 60 ml/min/1.73 m^2 and need tighter glycaemic control, the dose can be increased to 25 mg once daily. The maximum daily dose is 25 mg. When used with sulphonylurea or insulin a lower dose of these may be considered to reduce the risk of hypoglycaemia. *Renal impairment:* The glycaemic efficacy is dependent on renal function. No dose adjustment is required for patients with an eGFR ≥60 ml/min/1.73 m^2 or CrCl ≥60 ml/min. Do not initiate in patients with an eGFR <60 ml/min/1.73 m^2 or CrCl <60 ml/min. In patients tolerating empagliflozin whose eGFR falls persistently below 60 ml/min/1.73 m^2 or CrCl below 60 ml/min, the dose of empagliflozin should be adjusted to or maintained at 10 mg once daily. Discontinue when eGFR is persistently below 45 ml/min/1.73 m^2 or CrCl persistently below 45 ml/min. Not for use in patients with end stage renal disease (ESRD) or on dialysis. *Hepatic impairment:* No dose adjustment is required for patients with hepatic impairment. Not recommended in severe hepatic impairment. *Elderly patients:* No dose adjustment is recommended based on age. In patients 75 years and older, an increased risk for volume depletion should be taken into account. Not recommended in patients 85 years or older. *Paediatric population:* No data are available. *Method of administration:* The tablets can be taken with or without food, swallowed whole with water. If a dose is missed, it should be taken as soon as the patient remembers; however, a double dose should not be taken on the same day. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. **Warnings and Precautions:** Rare cases of diabetic ketoacidosis (DKA), including life-threatening and fatal cases, have been reported in patients treated with SGLT2 inhibitors, including empagliflozin. Consider the risk of DKA in the event of non-specific symptoms such as nausea, vomiting, anorexia, abdominal pain, excessive thirst, difficulty breathing, confusion, unusual fatigue or sleepiness and assess patients for ketoacidosis immediately, regardless of blood glucose level. In patients where DKA is suspected or diagnosed, treatment should be discontinued immediately. Treatment should be interrupted in patients who are hospitalised for major surgical procedures or acute serious medical illnesses. Monitoring of ketones is recommended in these patients. Measurement of blood ketone levels is preferred to urine. Treatment with empagliflozin may be restarted when the ketone values are normal and the patient's condition has stabilised. Before initiating empagliflozin, consider factors in the patient history that may predispose to ketoacidosis. Use with caution in patients who may be at higher risk of DKA. *Renal impairment:* See under Dose and Administration; Monitor renal function prior to initiation and at least annually. Cases of hepatic injury have been reported with empagliflozin in clinical trials. A causal relationship between empagliflozin and hepatic injury has not been established. Haematocrit increase was observed with empagliflozin treatment. Osmotic diuresis accompanying therapeutic glucosuria may lead to a modest decrease in blood pressure. Therefore, caution should be exercised in patients with known cardiovascular disease, patients on anti-hypertensive therapy with a history of hypotension or patients aged 75 years and older. In case of conditions that may lead to fluid loss (e.g. gastrointestinal illness), careful monitoring of volume status and electrolytes is recommended. Temporary interruption of treatment with empagliflozin should be considered until the fluid loss is corrected. *Elderly:* See under Dose and Administration; special attention should be given to volume intake of elderly patients in case of co-administered medicinal products which may lead to volume depletion (e.g. diuretics, ACE-inhibitors). Temporary interruption of empagliflozin should be considered in patients with complicated urinary tract infections. Cases of necrotising fasciitis of the perineum (Fournier's gangrene), have been reported in patients taking SGLT2 inhibitors. This is a rare but serious and potentially life-threatening event that requires urgent surgical intervention and antibiotic treatment. Patients should be advised to seek medical attention if they experience a combination of symptoms of pain, tenderness, erythema, or swelling in the genital or perineal area, with fever or malaise. Be aware that either uro-genital infection or perineal abscess may precede necrotising fasciitis. If Fournier's gangrene is suspected, Jardiance should be discontinued and prompt treatment should be instituted. An increase in cases of lower limb amputation (primarily of the toe) has been observed in long-term clinical studies with another SGLT2 inhibitor, counsel patients on routine preventative footcare. Experience in New York Heart Association (NYHA) class I-II is limited, and there is no experience in clinical studies with empagliflozin in NYHA class III-IV. Due to its mechanism of action, patients taking Jardiance will test positive for glucose in their urine. The tablets contain lactose and should not be used in patients with rare hereditary problems of galactose intolerance, total lactase deficiency, or glucose-galactose malabsorption. **Interactions:** Use with diuretics may increase the risk of dehydration and hypotension. Insulin and insulin secretagogues may increase the risk of hypoglycaemia therefore, a lower dose of insulin or an insulin secretagogue may be required. The effect of UGT induction on empagliflozin has not been studied. Co-treatment with known inducers of UGT enzymes should be avoided due to a potential risk of decreased efficacy. Interaction studies suggest that the pharmacokinetics of empagliflozin were not influenced by coadministration with metformin, glimepiride, pioglitazone, sitagliptin, linagliptin, warfarin, verapamil, ramipril, simvastatin, torasemide and hydrochlorothiazide. Interaction studies conducted in healthy volunteers suggest that empagliflozin had no clinically relevant effect on the pharmacokinetics of metformin, glimepiride, pioglitazone, sitagliptin, linagliptin, simvastatin, warfarin, ramipril, digoxin, diuretics and oral contraceptives. **Fertility, pregnancy and lactation:** There are no data from the use of empagliflozin in pregnant women. As a precautionary measure, it is preferable to avoid the use of Jardiance during pregnancy. No data in humans are available on excretion of empagliflozin into milk. Jardiance should not be used during breast-feeding. No studies on the effect on human fertility have been conducted for Jardiance. **Undesirable effects:** Frequencies are defined as very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), not known (cannot be estimated from the available data). Very common: hypoglycaemia (when used with sulphonylurea or insulin). Common: vaginal moniliasis, vulvovaginitis, balanitis and other genital infections, urinary tract infection (including pyelonephritis and urosepsis), thirst, pruritus (generalised), rash, increased urination, serum lipids increased. Uncommon: urticaria, volume depletion, dysuria, blood creatinine increased/glomerular filtration rate decreased, haematocrit increased. Rare: DKA. Not known: necrotising fasciitis of the perineum (Fournier's gangrene), angioedema. Prescribers should consult the Summary of Product Characteristics for further information on side effects. **Pack sizes:** 10 mg; 28 tablets, 25 mg: 28 tablets. **Legal category:** POM. **MA numbers:** 10 mg/28 tablets EU/1/14/930/013; 25 mg/28 tablets EU/1/14/930/004. **Marketing Authorisation Holder:** Boehringer Ingelheim International GmbH, D-55216 Ingelheim am Rhein, Germany. Prescribers should consult the Summary of Product Characteristics for full prescribing information. Additional information is available on request from Boehringer Ingelheim Ireland Ltd, The Crescent Building, Northwood, Santry, Dublin 9. **Prepared in October 2019**.

Adverse events should be reported. Reporting forms and information can be found at https://www.hpra.ie/homepage/about-us/report-an-issue. Adverse events should also be reported to Boehringer-Ingelheim Drug Safety on 01 2913960, Fax: +44 1344 742661, or by e-mail: PV_local_UK_Ireland@boehringer-ingelheim.com

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(empagliflozin)