PRESCRIBING INFORMATION

FORXIGA® (dapagliflozin) 5MG & 10MG FILM-COATED TABLETS.

Consult Summary of Product Characteristics (SmPC) before prescribing.

Indications: **Adults***:* For the treatment of insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise, as monotherapy when metformin is considered inappropriate due to intolerance, or in addition to other medicinal products for the treatment of type 2 diabetes. For the treatment of symptomatic chronic heart failure with reduced ejection fraction (HFrEF).

Presentation: Film-coated tablets. 5mg or 10mg of dapagliflozin (as propanediol monohydrate). Each 5mg tablet contains 25mg of lactose anhydrous. Each 10mg tablet contains 50mg of lactose anhydrous.

Dosage and Administration: **Adults: Type II Diabetes Mellitus:** The recommended dose is 10mg once daily. Forxiga can be taken at any time of day with or without food. Tablets should be swallowed whole. Consider a lower dose of insulin or insulin secretagogue such as a sulphonylurea when used in combination with dapagliflozin to reduce the risk of hypoglycaemia. **Heart Failure:** The recommended dose is 10mg once daily. **Children and adolescents:** <18 years: Safety and efficacy not yet established. **Elderly:** ≥65 years: No dosage adjustment is recommended based on age. **Renal impairment:** To improve glycaemic control, Forxiga is not to be initiated in patients with glomerular filtration rate (GFR) <60mL/min. Discontinue if GFR persistently below 45mL/min. No dosage adjustment required based on renal function. There is limited experience with dapagliflozin for the treatment of HFrEF in patients with severe renal impairment (GFR < 30 mL/min). **Mild or moderate hepatic impairment:** No dosage adjustment. **Severe hepatic impairment**: Starting dose of 5mg is recommended, if well tolerated, dose may be increased to 10mg. **Type I Diabetes Mellitus:** Forxiga 10 mg is not recommended for the treatment of heart failure in patients with type 1 diabetes mellitus.

Contraindications: Hypersensitivity to dapagliflozin, or excipients.

Warnings and Precautions: **Renal impairment:** In patients treated with dapagliflozin for both HFrEF and type 2 diabetes mellitus, additional glucose-lowering treatment should be considered if GFR falls persistently below 45 mL/min. **Renal impairment in Type II Diabetes Mellitus:** Renal function monitoring is recommended: prior to initiation of dapagliflozin and at least yearly thereafter; prior to initiation of concomitant medicinal products that may reduce renal function and periodically thereafter; for renal function with GFR <60 mL/min, at least 2 to 4 times per year. **Renal impairment in the treatment of heart failure**: There is limited experience with dapagliflozin for the treatment of HFrEF in patients with severe renal impairment (GFR < 30 mL/min). **Hepatic impairment:** Exposure is increased in patients with severe hepatic impairment. **Use in patients at risk of volume depletion and/or hypotension:** Dapagliflozin increases diuresis which may lead to a modest decrease in blood pressure, it may be more pronounced in patients with very high blood glucose concentrations. Exercise caution in patients for whom a dapagliflozin-induced drop in blood pressure could pose a risk, such as patients on anti-hypertensive therapy with a history of hypotension or elderly patients. Careful monitoring of volume status and electrolytes is recommended in conditions leading to volume depletion, such as acute gastrointestinal illness. In volume depleted patients temporary interruption of dapagliflozin is recommended until volume depletion is corrected. **Diabetic ketoacidosis (DKA):** SGLT2 inhibitors should be used with

caution in patients with increased risk of DKA. Patients who may be at higher risk of DKA include patients with a low beta-cell function reserve (e.g. patients with low C-peptide or latent autoimmune diabetes in adults (LADA) or patients with a history of pancreatitis), patients with conditions that lead to restricted food intake or severe dehydration, patients for whom insulin doses are reduced and patients with increased insulin requirements due to acute medical illness, surgery or alcohol abuse. The risk of DKA must be considered in the event of non-specific symptoms such as nausea, vomiting, anorexia, abdominal pain, excessive thirst, difficulty breathing, confusion, unusual fatigue or sleepiness. Patients should be assessed for ketoacidosis immediately if these symptoms occur, regardless of blood glucose level. Before initiating dapagliflozin, factors in patient history that may predispose to ketoacidosis should be considered. 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 patient's. Measurement of blood ketone level is preferred to urine. Treatment with dapagliflozin may be restarted when the ketone values are normal and the patient's condition has stabilised. Rare cases of DKA, including life-threatening and fatal cases, have been reported in patients treated with SGLT2 inhibitors, including dapagliflozin. In a number of cases, the presentation of the condition was atypical with only moderately increased blood glucose values, below 14mmol/L (250mg/dL). In patients where DKA is suspected or diagnosed, dapagliflozin treatment should be stopped immediately. Restarting SGLT2 inhibitor treatment in patients with previous DKA while on SGLT2 inhibitor treatment is not recommended, unless another clear precipitating factor is identified and resolved. **Necrotising fasciitis of the perineum (Fournier's gangrene):** Post-marketing cases have been reported in female and male patients taking SGLT2 inhibitors. Urgent surgical intervention and antibiotic treatment required. Advise patients to seek medical attention if they experience a combination of pain, tenderness, erythema, or swelling in the genital or perineal area, with fever or malaise. Either uro-genital infection or perineal abscess may precede necrotising fasciitis. If suspected discontinue Forxiga and institute prompt treatment (including antibiotics and surgical debridement). **Urinary tract infections:** Temporary interruption of dapagliflozin should be considered when treating pyelonephritis or urosepsis. **Elderly (≥65 years):** Elderly patients are more likely to have impaired renal function, be treated with medicines such as anti-hypertensives or diuretics, and be at a greater risk of volume depletion. **Cardiac failure:** Experience with dapagliflozin in NYHA class IV is limited. **Lower limb amputations:** Counsel patients with diabetes on routine preventative foot care. An increase in cases of lower limb amputation (primarily of the toe) has been observed in long-term, clinical studies with SGLT2 inhibitors. **Urine laboratory assessments:** Patients will test positive for glucose in the urine due to mechanism of action. **Lactose:** Patients with rare hereditary problems of galactose intolerance, total lactase deficiency, or glucose-galactose malabsorption should not take Forxiga.

Drug Interactions: **Diuretics**: Dapagliflozin may add to the diuretic effect of thiazide and loop diuretics and may increase the risk of dehydration and hypotension. **Insulin and insulin secretagogues**: Consider a lower dose of insulin or insulin secretagogue in combination with dapagliflozin to reduce the risk of hypoglycaemia. **Interference with 1,5-AG assay:** Monitoring glycaemic control with 1,5-AG assay is not recommended as measurements of 1,5-AG are unreliable in assessing glycaemic control in patients taking SGLT2 inhibitors. Alternative methods should be used.

Pregnancy and Lactation: Not recommended during the second and third trimesters of pregnancy. Treatment should be discontinued when pregnancy is detected. Do not use whilst breast-feeding.

Ability to Drive and Use Machines: Alert patients on the risk of hypoglycaemia when dapagliflozin is used in combination with a sulphonylurea or insulin.

Undesirable Events: Consult SmPC for full list of side effects. **Very common** (≥1/10): Hypoglycaemia (when used with SU or insulin). **Common** (≥1/100 to <1/10): Vulvovaginitis, balanitis and related genital infections, urinary tract infection, dizziness, rash, back pain, dysuria, polyuria, haematocrit increased, creatinine renal clearance decreased during initial treatment, dyslipidaemia. **Uncommon** (≥1/1,000 to < 1/100): Volume depletion. **Rare** (≥ 1/10,000 to < 1/1,000): Diabetic ketoacidosis. **Very Rare** (< 1/10,000): Angioedema, necrotising fasciitis of the perineum (Fournier's gangrene).

Legal Category: POM.

Marketing Authorisation Number: EU/1/12/795/002; EU/1/12/795/007.

Presentation & Basic NHS Cost: Forxiga 5mg film-coated tablets 28: £36.59; Forxiga 10mg film-coated tablets 28: £36.59.

Marketing Authorisation Holder: AstraZeneca AB, SE-151 85 Södertälje, Sweden.

Further Information is Available From: AstraZeneca UK Ltd., 600 Capability Green, Luton, LU1 3LU, UK.

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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 AstraZeneca by visiting https://aereporting.astrazeneca.com or by calling 0800 783 0033.