Forxiga (dapagliflozin) in heart failure (HFrEF): key considerations for prescribers

Forxiga is indicated in adults for the treatment of symptomatic chronic heart failure with reduced ejection fraction (HFrEF) and for the treatment of insufficiently controlled type 2 diabetes (T2D).

See SmPC for detailed information. Prescribing information can be found on page 5.

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### Simple Dosing

| 10 mg | Once daily | No uptitratation* |

*In patients with severe hepatic impairment, a starting dose of 5 mg is recommended. If well tolerated, the dose may be increased to 10 mg.

### GFR Considerations

- No dose adjustment is required based on renal function
- For the treatment of heart failure (HFrEF), no requirement to stop Forxiga if GFR falls below 30 mL/min. There is limited experience in patients with GFR below 30 mL/min

### Type 1 or Type 2 Diabetes

- Forxiga is indicated for the treatment of type 1 diabetes (T1D), however, not recommended for the treatment of heart failure in patients with T1D
- If unsure of diabetes type, refer to your diabetes team

### Key Considerations for Concomitant Therapies

- Do not routinely reduce dose of diuretic therapy
- Diuretics were not routinely adjusted in the DAPA-HF trial and volume depletion was not a safety signal\(^2\),\(^3\)
- Adjustments should be based on clinical judgment and tailored to patient requirements

### Impact of Glucose-Lowering Treatments

**For patients with heart failure (HFrEF) and T2D**

- **Low risk of hypoglycaemia with Forxiga and these agents**\(^1\)
  - Metformin
  - DPP4is or Gliptins
    - alogliptin, linagliptin, sitagliptin, saxagliptin, and vildaglaptin
  - GLP-1 receptor agonists
    - dulaglutide, exenatide, liraglutide, lixisenatide and semaglutide

**Increased risk of hypoglycaemia when Forxiga is administered with these agents**\(^1\)

- Insulin
- Sulphonylurea (SU)
  - glibenclamide, gliclazide, glimepiride, glipizide, tolbutamide

**When to consider insulin or SU dose adjustments**\(^1\)

- A lower dose of insulin or SU may be considered to reduce the risk of hypoglycaemia

**Considerations for glycaemic control**\(^1\)

- Glucose-lowering effect of Forxiga is dependent on renal function and is likely to be limited in GFR below 45 mL/min
- Additional glucose-lowering therapy should be considered if GFR falls persistently below 45 mL/min
CONSIDERATIONS AT FOLLOW-UP

- Monitor blood pressure, urea and electrolytes as you would for monitoring requirements of other heart failure treatments.
- For patients with T2D, monitor renal function prior to initiation and at least yearly thereafter.
  - Remember – slight decrease in GFR for first few months is normal.
- In cases of intercurrent conditions that may lead to volume depletion, careful monitoring of volume status is recommended.
PATIENT COUNSELLING FOR POTENTIAL SIDE EFFECTS

Genital/perineal hygiene

- With Forxiga, fungal genital infections (thrush) are common in patients with T2D
- Counsel the patient on risk/symptoms and encourage personal hygiene
- Most cases are mild to moderate and can be managed with a short course of antifungal cream or oral treatment
- Those with prior history are more likely to have recurring infection

Symptoms of diabetic ketoacidosis (DKA)

- DKA is a rare but serious side effect. In a number of DKA cases reported with SGLT2 inhibitors, presentation was atypical with only moderately increased blood glucose values (below 14 mmol/L)
- Awareness is important. Symptoms include:
  - Feeling and/or being sick
  - Drowsiness/confusion
  - Sweet-smelling breath (like pear drops or acetone)
  - Thirst
  - Stomach pain
  - Rapid weight loss
  - Deep sighing breaths
- Higher risk if dehydrated, fasting, have an infection or have alcohol dependency
- DKA should be treated in hospital as soon as possible
- Due to the risk of DKA, advise patients with T2D to follow ‘sick day rules’ if they have an acute dehydrating illness, infection or are undergoing surgery
  - Temporarily withhold Forxiga for this period then RESTART when patient feeling better (eating and drinking normally)
- Routine ketone monitoring is not required (monitoring is recommended in patients undergoing major surgical procedures or acute serious medical illnesses)
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 in the treatment of HFrEF in patients with severe renal impairment (GFR <30mL/ 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 by 10mg. Type 1 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. Additional monitoring treatment and dosage adjustment 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 <30mL/min). No additional monitoring treatment or dosage adjustment should be considered when GFR falls persistently below 45 mL/min. 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. Elderly, 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 (≥10%): Hypoglycaemia (when used with SU or insulin). Common (≥1/100 to <1/10): Vomiting, diarrhoea, flatulence, dizziness, 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/117/795/002; EU/117/795/007. 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. FORXIGA is a trademark of the AstraZeneca group of companies. Date of preparation: 11/2020.

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://contactazmedical. astrazeneca.com or by calling 0800 783 0033.