FORXIGA® (dapagliflozin) Therapy in Heart Failure with Reduced Ejection Fraction (HFrEF)[1]

FORXIGA is indicated in adults, as an adjunct to standard of care therapy, for the treatment of HFrEF to reduce the risk of cardiovascular (CV) death, hospitalization for heart failure and urgent heart failure visit.

PRE-INITIATION ASSESSMENT
A SELECTED PRESENTATION OF INFORMATION

VOLUME STATUS

In patients with evidence of volume depletion, this condition should be corrected prior to initiation of FORXIGA.

RENAL FUNCTION

There is limited experience with FORXIGA in patients with severe renal impairment (eGFR <30 mL/min/1.73 m^2) or ESRD. FORXIGA is contraindicated in patients with an eGFR <30 mLmin/1.73 m^2, ESRD or patients on dialysis.

HYPOTENSION

Caution should be exercised in patients for whom a dapagliflozin induced drop in blood pressure could pose a risk, such as elderly patients, patients with low systolic blood pressure or moderate renal impairment, or in case of intercurrent conditions that may lead to volume depletion (such as gastrointestinal illness).*

RECOMMENDED DOSE

10 mg once daily

Can be taken any time of the day

With or without food

In the DAPA-HF study, FORXIGA was used in conjunction with other heart failure therapies.

PATIENT COUNSELLING

- Awareness of signs/symptoms of volume depletion, diabetic ketoacidosis, genital mycotic infections, urosepsis/pyelonephritis and Fournier's gangrene
- Patients, particularly those with a history of genital mycotic infections, should be advised that FORXIGA increases the risk of genital mycotic infections
- Educate on appropriate genital/perineal hygiene

Monitor for hypotension, renal function, volume depletion

Use in patients at risk for volume depletion, hypotension and/or electrolyte imbalances:
Due to its mechanism of action, dapagliflozin causes osmotic diuresis that may be associated with decreases in blood pressure, which may be more pronounced in patients with high blood glucose concentrations.

Assess patients with diabetes for DKA

DKA, a serious life-threatening condition requiring urgent hospitalization, have been reported in patients with T2DM taking FORXIGA. In a number of reported cases, the presentation of the condition was atypical with only moderately increased blood glucose values below 13.9 mmol/L. Some cases of DKA have been fatal.

Assess for DKA immediately if non-specific symptoms such as difficulty breathing, nausea, vomiting, abdominal pain, confusion, anorexia, excessive thirst and unusual fatigue or sleepiness occur, regardless of blood glucose level.

Evaluate for signs and symptoms of genito-urinary infections and Fournier's gangrene

Treatment with FORXIGA increases the risk of genital mycotic infections and urinary tract infections. There have been post-marketing reports of serious urinary tract infections, including urosepsis and pyelonephritis, requiring hospitalization in patients treated with FORXIGA.

Evaluate patients for signs and symptoms of urinary tract infections and treat promptly, if indicated.

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Caution should be exercised in patients for whom a dapagliflozin induced drop in blood pressure could pose a risk, such as elderly patients, patients with low systolic blood pressure or moderate renal impairment, or in case of intercurrent conditions that may lead to volume depletion (such as gastrointestinal illness).

Careful monitoring of volume status is recommended. Temporary interruption of FORXIGA may be considered for patients who develop volume depletion until the depletion is corrected.

Renal function: Initiation of FORXIGA may transiently increase serum creatinine and decreases eGFR in a dose dependent fashion. In clinical trials, renal function abnormalities have occurred after initiating FORXIGA.

If DKA is suspected, patients should discontinue FORXIGA treatment and be assessed for DKA immediately.

If DKA is diagnosed, FORXIGA should be discontinued immediately.

FORXIGA should not be used for the treatment of DKA or in patients with a history of DKA.

FORXIGA should not be used in patients with type 1 diabetes.

Patients with conditions that can precipitate DKA (which include a very low carbohydrate diet as the combination may further increase ketone body production, dehydration, high alcohol consumption and a low beta-cell function reserve) while taking FORXIGA should be monitored closely.

Caution should be taken when reducing the insulin dose in patients requiring insulin.

Interruption of treatment with FORXIGA should be considered in T2DM patients who are hospitalized for major surgical procedures, serious infections or acute serious medical illness.

Post-marketing cases of necrotizing fasciitis of perineum (Fournier's gangrene), a rare but serious and potentially life-threatening necrotizing infection requiring urgent surgical intervention, have been reported in female and male patients with diabetes mellitus receiving SGLT2 inhibitors, including FORXIGA. Serious outcomes have included hospitalization, multiple surgeries, and death.

Patients treated with FORXIGA who present with pain or tenderness, erythema, or swelling in the genital or perineal area, with or without fever or malaise, should be evaluated for necrotizing fasciitis (Fournier's gangrene). If suspected, FORXIGA should be discontinued and prompt treatment should be instituted (including broad-spectrum antibiotics and surgical debridement if necessary).

Please see the Product Monograph for complete dosing and administration information and for additional warnings and precautions.

Renal impairment:
Heart Failure (DAPA-HF): No dosage adjustment is required based on renal function. FORXIGA is contraindicated in patients with an eGFR less than 30 mL/min/1.73 m^2, ESRD or patients on dialysis.

Please see the Product Monograph for complete dosing and administration information.

Consult the product monograph at www.azinfo.ca/forxiga/pm367 for important information about:

- Contraindications in patients with an estimated glomerular filtration rate (eGFR) less than 30 mL/min/1.73 m^2, end-stage renal disease (ESRD) or patients on dialysis
- The most serious warning and precaution regarding diabetic ketoacidosis (DKA) in patients with diabetes
- Other relevant warnings and precautions regarding: DKA in patients with diabetes; use in patients at risk for volume depletion, hypotension and/or electrolyte imbalances; hypoglycemia; dose-related LDL-C increases; increased mean hemoglobin/hematocrit and frequency of patients with abnormally elevated values of hemoglobin/hematocrit; genital mycotic infections and urinary tract infections (including urosepsis and pyelonephritis); necrotizing fasciitis of the perineum (Fournier's gangrene); severe hepatic impairment; renal function abnormalities; in patients with T2D: acute kidney injury, including acute renal failure, patients with hypovolemia, renal function; patients with severe renal impairment (eGFR <30 mL/min/1.73 m^2), or ESRD; use in pregnant or nursing women; testing positive for glucose in urine

The Product Monograph is also available by calling 1-800-668-6000.

CV: cardiovascular; DAPA-HF: Dapagliflozin and Prevention of Adverse Outcomes in Heart Failure; DKA: diabetic ketoacidosis; eGFR: estimated glomerular filtration rate; ESRD: end-stage renal disease; HFrEF: heart failure with reduced ejection fraction; T2D: type 2 diabetes.

REFERENCE: 1. FORXIGA Product Monograph. AstraZeneca Canada Inc. June 29, 2020.

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REVIEWED BY PAAB

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