DAPAFOX 10 TABLETS
Dapagliflozin Tablets 10 mg

PRODUCT NAME: Dapagliflozin Tablets 10 mg
NAME AND STRENGTH OF ACTIVE INGREDIENT (S): Dapagliflozin 10 mg
Description: Yellow coloured, round shape, biconvex film coated tablets plain on both sides.
PHARMACOLOGICAL CLASSIFICATION: Dapagliflozin is classified as a sodium-glucose co-transporter 2 (SGLT2) inhibitor. This class of drugs is a type of oral anti-diabetic agent that works independently of insulin.
PHARMACODYNAMICS/ PHARMACOKINETICS:
Pharmacodynamics:
Pharmacotherapeutic Group: Hypoglycemic agent/Antidiabetic drug.
ATC code: A10BK01
Mechanism of action:
Inhibition of SGLT2 by dapagliflozin reduces reabsorption of glucose from the glomerular filtrate in the proximal renal tubule with a concomitant reduction in sodium reabsorption leading to urinary excretion of glucose and osmotic diuresis. Dapagliflozin therefore increases the delivery of sodium to the distal tubule which is believed to increase tubule-glomerular feedback and reduce intraglomerular pressure.
Pharmacokinetics:
Absorption
Dapagliflozin was rapidly and well absorbed after oral administration. Maximum dapagliflozin plasma concentrations (Cmax) were usually attained within 2 hours after administration in the fasted state.
Distribution
Dapagliflozin is approximately 91% protein bound. Protein binding was not altered in various disease states (e.g., renal or hepatic impairment). The mean steady-state volume of distribution of dapagliflozin was 118 liters.
Biotransformation
Dapagliflozin is extensively metabolized, primarily to yield dapagliflozin 3-O-glucuronide, which is an inactive metabolite. Dapagliflozin 3-O-glucuronide or other metabolites do not contribute to the glucose-lowering effects.
Elimination
The mean plasma terminal half-life (t1/2) for dapagliflozin was 12.9 hours following a single oral dose of dapagliflozin 10 mg to healthy subjects. The mean total systemic clearance of dapagliflozin administered intravenously was 207 mL/min. Dapagliflozin and related metabolites are primarily eliminated via urinary excretion with less than 2% as unchanged dapagliflozin.
RECOMMENDED DOSE:
Type 2 Diabetes mellitus: Recommended dose is 10 mg once daily.
Type 1 Diabetes mellitus: Treatment is to be initiated & supervised by specialist
Recommended dose is 10 mg once a day.
Heart failure: The recommended dose is 10 mg dapagliflozin once daily.
Special population
Treatment of diabetes mellitus in patients with renal impairment: Dapagliflozin should not be initiated to improve glycaemic control in patients with a glomerular filtration rate [GFR] < 60 mL/min and should be discontinued at GFR persistently below 45 mL/min. No dose adjustment needed based on renal function.
Treatment of heart failure in patients with renal impairment: No dose adjustment needed based on renal function.
Hepatic impairment: No dose adjustment is necessary for patients with mild or moderate hepatic impairment.
Elderly (≥ 65 years): No dose adjustment needed.
Paediatric population: The safety and efficacy of dapagliflozin in children aged 0 to < 18 years have not yet been established. No data are available.
Method of administration
Oral administration (Tablet)
CONTRA-INDICATIONS:
Hypersensitivity to the active substance or to any of the excipients.
WARNING AND PRECAUTIONS:
Treatment of Diabetes mellitus: The glycaemic efficacy of dapagliflozin is dependent on renal function, and efficacy is reduced in patients who have moderate renal impairment and is likely absent in patients with severe renal impairment.
Renal function monitoring is recommended as follows:
Prior to initiation of Dapagliflozin & at least yearly, thereafter.
Prior to initiation of concomitant medicinal products that may reduce renal function & periodically thereafter.
For renal function with GFR < 60 ml/min, at least 2-4 times per year.
Treatment of heart failure: There is limited experience with dapagliflozin for the treatment of heart failure in patients with severe renal impairment (GFR < 30 mL/min).
Hepatic impairment: There is limited experience in clinical studies in patients with hepatic impairment. Dapagliflozin exposure is increased in patients with severe hepatic impairment.
Use in patients at risk for volume depletion and/or hypotension: Due to its mechanism of action, dapagliflozin increases diuresis which may lead to the modest decrease in blood pressure observed in clinical studies.
Diabetic Ketoacidosis: Sodium-glucose co-transporter 2 (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. type 1 diabetes patients, type 2 diabetes patients with low C-peptide or latent autoimmune diabetes in adults (LADA) or patients with a history of pancreatitis).
Type 2 Diabetes mellitus: Rare cases of DKA, including life-threatening and fatal cases, have been reported in patients treated with SGLT2 inhibitors, including dapagliflozin.
Type 1 Diabetes mellitus: Dapagliflozin has not been studied for the treatment of heart failure in patients with type 1 diabetes mellitus. Treatment of these patients with dapagliflozin 10 mg is not recommended.
Necrotising fasciitis of the perineum (Fournier's gangrene): Post-marketing cases of necrotising fasciitis of the perineum (also known as Fournier's gangrene) have been reported in female and male patients taking SGLT2 inhibitors. 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.
Urinary tract infections: As with other vasodilators, special caution is indicated in patients suffering from aortic or mitral stenosis, or obstructive hypertrophic cardiomyopathy.
Diabetic patients treated with insulin or antidiabetics: Urinary glucose excretion may be associated with an increased risk of urinary tract infection; therefore, temporary interruption of dapagliflozin should be considered when treating pyelonephritis or urosepsis.
Elderly (≥ 65 years): Elderly patients may be at a greater risk for volume depletion and are more likely to be treated with diuretics.
Cardiac failure: Experience with dapagliflozin in NYHA class IV is limited.
Lower limb amputation: An increase in cases of lower limb amputation (primarily of the toe) has been observed in long-term, clinical studies in type 2 diabetes mellitus with SGLT2 inhibitors.

INTERACTIONS WITH OTHER MEDICINAL PRODUCTS:
Diuretics: Dapagliflozin may add to the diuretic effect of thiazide and loop diuretics and may increase the risk of dehydration and hypotension.
Insulin & insulin secretagogues: a lower dose of insulin or an insulin secretagogue may be required to reduce the risk of hypoglycaemia when used in combination with dapagliflozin in patients with type 2 diabetes mellitus.
Pharmacokinetic interactions: Dapagliflozin is not expected to alter the metabolic clearance of co-administered medicinal products that are metabolised by enzymes like CYPP450, (CYP) 1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP3A4, CYP1A2, CYP2B6 or CYP3A4.
Effects of other medicinal products on Dapagliflozin: The pharmacokinetics of dapagliflozin are not altered by metformin, pioglitazone, sitagliptin, glimepiride, voglibose, hydrochlorothiazide, bumetanide, valsartan, or simvastatin.
Effect of Dapagliflozin on other medicinal products: Dapagliflozin did not alter the pharmacokinetics of metformin, pioglitazone, sitagliptin, glimepiride, hydrochlorothiazide, bumetanide, valsartan, digoxin (a P-gp substrate) or warfarin (S-warfarin, a CYP2C9 substrate), or the anticoagulatory effects of warfarin as measured by INR.
Interference with 1,5-anhydroglucitol (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. Use of alternative methods to monitor glycaemic control is advised.
Paediatric population: Interaction studies have only been performed in adults.
PREGNANCY AND LACTATION:
Pregnancy
The use of dapagliflozin is not recommended during the second and third trimesters of pregnancy.
When pregnancy is detected, treatment with dapagliflozin should be discontinued.
Lactation
It is unknown whether dapagliflozin and/or its metabolites are excreted in human milk. A risk to the new-borns/infants cannot be excluded. Dapagliflozin should not be used while breast-feeding.
Fertility
The effect of dapagliflozin on fertility in humans has not been studied.
UNDESIRABLE EFFECTS:
Type 2 Diabetes mellitus: The most frequently reported adverse reactions across the clinical studies were genital infections.
Type 1 Diabetes mellitus: The safety profile of dapagliflozin in subjects with type 1 diabetes mellitus was similar to the known safety profile of dapagliflozin in subjects with type 2 diabetes mellitus. In patients with type 1 diabetes mellitus, diabetic ketoacidosis was reported with common frequency.
Heart failure: The overall safety profile of dapagliflozin in patients with heart failure was consistent with the known safety profile of dapagliflozin.
Infections and infestations
Common: Vulvovaginitis, balanitis & related genital infections, UTI
Uncommon: Fungal infection
Very rare: Necrotising fasciitis of the perineum (Fournier's gangrene)
Metabolism and nutrition disorders
Very common: Hypoglycaemia (when used with SU/insulin)
Common: Diabetic Ketoacidosis (DKA) (when used in Type 1 Diabetes mellitus)
Uncommon: Volume depletion, thirst
Rare: DKA (when used in Type 2 Diabetes mellitus)
Nervous system disorders
Common: Dizziness
Gastrointestinal disorders
Uncommon: Constipation, dry mouth
Skin and subcutaneous tissue disorders
Common: Rash
Very rare: Angioedema
Musculoskeletal and connective tissue disorders
Common: Back pain
Rare: Arthralgia, pain in extremity, tendon pain (tendonitis like symptoms)
Renal and urinary disorders
Common: Dysuria, Polyuria
Uncommon: Nocturia
Reproductive system & breast disorders
Uncommon: Vulvovaginal pruritus, pruritus genital
Investigations
Common: Haematocrit increased, creatinine renal clearance decreased during initial treatment, dyslipidemia
Uncommon: Blood creatinine increased during initial treatment, blood urea increased, weight decreased.
OVERDOSAGE AND TREATMENT:
In the event of an overdose, appropriate supportive treatment should be initiated as dictated by the patient's clinical status. The removal of dapagliflozin by haemodialysis has not been studied.
STORAGE CONDITION:
Store protected from light & moisture at a temperature not exceeding 30°C.
DOSAGE FORMS AND PACKAGING AVAILABLE:
ALU-ALU Packing of 10 X l0 Tablets
SHELF LIFE:
24 months

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