DAPXI Tablets

(Dapagliflozin)

ڈیپزی ٹیبلیٹس

(ڈاپاگلائی فلوزن)

COMPOSITION:

Dapxi 5mg Tablets

Each film coated tablet contains:

Dapagliflozin Propanediol Monohydrate eq. to Dapagliflozin ..... 5mg. [Innovator's Specs.]

Dapxi 10mg Tablets

Each film coated tablet contains:

Dapagliflozin Propanediol Monohydrate eq. to Dapagliflozin ... 10mg. [Innovator's Specs.]

DESCRIPTION: Dapagliflozin is described chemically as D-glucitol, 1,5-anhydro-1-C-[4-chloro-3-[(4-ethoxyphenyl)methyl]phenyl]-, (1S)-, compounded with (2S)-1,2-propanediol, hydrate (1:1:1). The empirical formula is $C_{21}H_{25}C_1O_6 \cdot C_3H_8O_2 \cdot H_2O$.

INDICATIONS:

Type 2 Diabetes Mellitus: Dapxi is indicated in adults and children aged 10 years and above 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.
- In addition to other medicinal products for the treatment of type 2 diabetes.

Heart Failure: Dapxi is indicated in adults for the treatment of symptomatic chronic heart failure with reduced ejection fraction.

Chronic Kidney Disease: Dapxi is indicated in adults for the treatment of chronic kidney disease.

DOSAGE AND ADMINISTRATION:

Type 2 Diabetes Mellitus: The recommended dose is 10mg Dapagliflozin once daily. When Dapagliflozin is used in combination with insulin or an insulin secretagogue, such as a sulphonylurea, a lower dose of insulin or insulin secretagogue may be considered to reduce the risk of hypoglycaemia.

Heart failure: The recommended dose is 10mg Dapagliflozin once daily.

Chronic kidney disease: The recommended dose is 10mg Dapagliflozin once daily.

SPECIAL POPULATIONS:

Renal impairment: No dose adjustment is required based on renal function. It is not recommended to initiate treatment with Dapagliflozin in patients with an estimated glomerular filtration rate (eGFR) < 15ml/min/1.73m^2.

Hepatic impairment: No dose adjustment is necessary for patients with mild or moderate hepatic impairment. In patients with severe hepatic impairment, a starting dose of 5mg is recommended. If well tolerated, the dose may be increased to 10mg.

Elderly (≥65 years): No dose adjustment is recommended based on age.

Paediatric population: No dose adjustment is required for the treatment of type 2 diabetes mellitus in children aged 10 years and above. No data are available for children below 10 years of age.

Method of administration: Dapxi can be taken orally once daily at any time of day with or without food. Tablets are to be swallowed whole.

CLINICAL PHARMACOLOGY:

Mechanism of Action: Sodium-glucose cotransporter 2 (SGLT2), expressed in the proximal renal tubules, is responsible for the majority of the reabsorption of filtered glucose from the tubular lumen. Dapagliflozin is an inhibitor of SGLT2. By inhibiting SGLT2, Dapagliflozin reduces reabsorption of filtered glucose and lowers the renal threshold for glucose, and thereby increases urinary glucose excretion.

PHARMACOKINETICS:

Absorption: Dapagliflozin was rapidly and well absorbed after oral administration. Maximum Dapagliflozin plasma concentrations (C_{max}) were usually attained within 2 hours after administration in the fasted state. Geometric mean steady-state Dapagliflozin C_{max} and AUC_τ values following once daily 10mg doses of Dapagliflozin were 158ng/ml and 628ng h/ml, respectively. The absolute oral bioavailability of Dapagliflozin following the administration of a 10mg dose is 78%. Administration with a high-fat meal decreased Dapagliflozin C_{max} by up to 50% and prolonged T_{max} by approximately 1 hour, but did not alter AUC as compared with the fasted state. These changes are not considered to be clinically meaningful. Hence, **Dapxi** can be administered with or without food.

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 metabolised, 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. The formation of Dapagliflozin 3-O-glucuronide is mediated by UGT1A9, an enzyme present in the liver and kidney, and CYP-mediated metabolism was a minor clearance pathway in humans.

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Elimination: The mean plasma terminal half-life ($t_{1/2}$) for Dapagliflozin was 12.9 hours following a single oral dose of Dapagliflozin 10mg to healthy subjects. The mean total systemic clearance of Dapagliflozin administered intravenously was 207ml/min. Dapagliflozin and related metabolites are primarily eliminated via urinary excretion with less than 2% as unchanged Dapagliflozin. After administration of a 50mg Dapagliflozin dose, 96% was recovered, 75% in urine and 21% in faeces. In faeces, approximately 15% of the dose was excreted as parent drug.

CONTRAINDICATIONS: Hypersensitivity to the active substance or to any of the excipients.

WARNINGS AND PRECAUTIONS:
Renal Impairment: Due to limited experience, it is not recommended to initiate treatment with Dapagliflozin in patients with GFR < 25ml/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. It may be more pronounced in patients with very high blood glucose concentrations.
Diabetic Ketoacidosis: Sodium-glucose co-transporter 2 (SGLT2) inhibitors should be used with caution in patients with increased risk of diabetic ketoacidosis (DKA).
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.
Pregnancy and Lactation: If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine. You should stop taking this medicine if you become pregnant, since it is not recommended during the second and third trimesters of pregnancy. Talk to your doctor about the best way to control your blood sugar while you are pregnant. Talk to your doctor if you would like to or are breast-feeding before taking this medicine. Do not use Dapagliflozin if you are breast-feeding. It is not known if this medicine passes into human breast milk.

SIDE EFFECTS:
Angioedema: Seen very rarely (may affect up to 1 in 10,000 people).
These are signs of angioedema: - Swelling of the face, tongue or throat. - Difficulties in swallowing. - Hives and breathing problems.
Diabetic Ketoacidosis: This is common in patients with type 1 diabetes (may affect up to 1 in 10 people) and rare in patients with type 2 diabetes (may affect up to 1 in 1,000 people).
These are the signs of diabetic ketoacidosis: - Increased levels of ketone bodies in your urine or blood. - Feeling sick or being sick. - Stomach pain. - Excessive thirst. - Fast and deep breathing. - Confusion. - Unusual sleepiness or tiredness. - A sweet smell to your breath, a sweet or metallic taste in your mouth or a different odour to your urine or sweat. - Rapid weight loss. This may occur regardless of blood sugar level. Your doctor may decide to temporarily or permanently stop your treatment with Dapagliflozin.
Necrotising Fasciitis of The Perineum or Fournier's gangrene: A serious soft tissue infection of the genitals or the area between the genitals and the anus, seen very rarely.
Serious Side Effects: Urinary Tract Infection: Seen commonly (may affect up to 1 in 10 people). These are signs of a severe infection of the urinary tract: - Fever and/or chills - Burning sensation when passing water (urinating) - Pain in your back or side.
Common Side Effects: Low Blood Sugar Levels (hypoglycaemia): Seen very commonly (may affect more than 1 in 10 people) in patients with diabetes taking this medicine with a sulphonylurea or insulin. These are the signs of low blood sugar - Shaking, sweating, feeling very anxious, fast heart beat. - Feeling hungry, headache, change in vision. - A change in your mood or feeling confused.

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: Insulin and insulin secretagogues, such as sulphonylureas, cause hypoglycaemia. Therefore, 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.

OVERDOSE: Dapagliflozin did not show any toxicity in healthy subjects at single oral doses up to 500mg (50 times the maximum recommended human dose).

INSTRUCTIONS: Store below 30° C. Protect from heat, light and moisture. Keep out of the reach of children.

PRESENTATION:
Dapxi 5mg and 10mg Tablets are available in a Blister pack of 10's.

ہدایات: ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔ گرمی، روشنی اور نمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔

Manufactured by:
NABIQASIM INDUSTRIES (PVT.) LTD.
PHARMA 17/24, Korangi Industrial Area, Karachi-Pakistan.
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