Dapaglu Tablets*

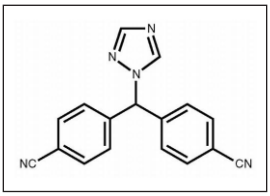
ڈیپاگلو ٹیبلٹس

COMPOSITION:

Each tablet contains: .....Dapagliflozin Propanediol Monohydrate* 5 &10 mg

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 C21H25ClO6C3H8O2H2O



CLNICAL 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

Following oral administration of dapagliflozin, the maximum plasma concentration (C max) is usually attained within 2 hours under fasting state. The C max and AUC values increase dose proportionally with increase in dapagliflozin dose in the therapeutic dose range. The absolute oral bioavailability of dapagliflozin following the administration of a 10 mg dose is 78%. Administration of dapagliflozin with a high-fat meal decreases its Cmax by up to 50% and prolongs T max by approximately 1 hour, but does not alter AUC as compared with the fasted state. These changes are not considered to be clinically meaningful and dapagliflozin can be administered with or without food.

Distribution

Dapagliflozin is approximately 91% protein bound. Protein binding is not altered in patients with renal or hepatic impairment.

Metabolism

The metabolism of dapagliflozin is primarily mediated by UGT1A9; CYP-mediated metabolism is a minor clearance pathway in humans. Dapagliflozin is extensively metabolized, primarily to yield dapagliflozin 3-O-glucuronide, which is an inactive metabolite.

Elimination

Dapagliflozin and related metabolites are primarily eliminated via the renal pathway. The mean plasma terminal half-life (t½) for dapagliflozin is approximately 12.9 hours following a single oral dose of DAPAGLU 10mg.

Pharmacodynamics

Cardiac Electrophysiology

Dapagliflozin is not associated with clinically meaningful prolongation of QTc interval at daily doses up to 150 mg (15 times the recommended maximum dose) in a study of healthy subjects. In addition, no clinically meaningful effect on QTc interval is observed following single doses of up to 500 mg (50 times the recommended maximum dose) of dapagliflozin in healthy subjects.

INDICATIONS AND USAGE

DAPAGLU (dapagliflozin) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitation of Use

DAPAGLU is not recommended for patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.

CONTRAINDICATIONS

History of a serious hypersensitivity reaction to DAPAGLU.

Severe renal impairment, end-stage renal disease (ESRD), or patients on dialysis.

ADVERSE REACTIONS

The most common adverse reactions associated with DAPAGLU (5% or greater incidence) are female genital mycotic infections, nasopharyngitis, and urinary tract infections.

DRUG INTERACTIONS

Positive Urine Glucose Test

Monitoring glycemic control with urine glucose tests is not recommended in patients taking SGLT2 inhibitors as SGLT2 inhibitors increase urinary glucose excretion and will lead to positive urine glucose tests. Use alternative methods to monitor glycemic control.

Interference with 1,5-anhydroglucitol (1,5-AG) Assay

Monitoring glycemic control with 1,5-AG assay is not recommended as measurements of 1,5 AG are unreliable in assessing glycemic control in patients taking SGLT2 inhibitors. Use alternative methods to monitor glycemic control.

WARNINGS AND PRECAUTIONS

Hypotension

DAPAGLU causes intravascular volume contraction. Symptomatic hypotension can occur after initiating DAPAGLU particularly in patients with impaired renal function (eGFR less than 60 mL/min/1.73 m2), elderly patients, or patients on loop diuretics. Before initiating DAPAGLU in patients with one or more of these characteristics, volume status should be assessed and corrected. Monitor for signs and symptoms of hypotension after initiating therapy.

Impairment in Renal Function

DAPAGLU increases serum creatinine and decreases eGFR. Elderly patients and patients with impaired renal function may be more susceptible to these changes.

Hypoglycemia with Concomitant Use with Insulin and Insulin Secretagogues

Insulin and insulin secretagogues are known to cause hypoglycemia. DAPAGLU can increase the risk of hypoglycemia when combined with insulin or an insulin secretagogue. Therefore, a lower dose of insulin or insulin secretagogue may be required to minimize the risk of hypoglycemia when these agents are used in combination with DAPAGLU.

Genital Mycotic Infections

DAPAGLU increases the risk of genital mycotic infections. Patients with a history of genital mycotic infections were more likely to develop genital mycotic infections. Monitor and treat appropriately.

Increases in Low-Density Lipoprotein Cholesterol (LDL-C)

Increases in LDL-C occur with DAPAGLU. Monitor LDL-C and treat per standard of care after initiating DAPAGLU.

Special Populations

Pregnancy

Pregnancy Category C

There are no adequate and well-controlled studies of DAPAGLU in pregnant women. During pregnancy, consider appropriate alternative therapies, especially during the second and third trimesters. DAPAGLU should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers

It is not known whether DAPAGLU is excreted in human milk. Many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from DAPAGLU, a decision should be made whether to discontinue nursing or to discontinue DAPAGLU, taking into account the importance of the drug to the mother.

Pediatric Use

Safety and effectiveness of DAPAGLU in pediatric patients under 18 years of age have not been established.

Geriatric Use

No DAPAGLU dosage change is recommended based on age.

Hepatic Impairment: No dose adjustment is recommended for patients with mild, moderate, or severe hepatic impairment. However, the benefit-risk for the use of dapagliflozin in patients with severe hepatic impairment should be individually assessed since the safety and efficacy of dapagliflozin have not been specifically studied in this population.

Renal Impairment

Patients with moderate renal impairment treated with DAPAGLU did not have improvement in glycemic control and had more renal-related adverse reactions and more bone fractures therefore, DAPAGLU should not be initiated in this population. Based on its mechanism of action, DAPAGLU is not expected to be effective in patients with severe renal impairment (eGFR less than 30 mL/min/1.73 m^2) or ESRD.

DOSAGE AND ADMINISTRATION

Recommended Dosing

The recommended starting dose of DAPAGLU is 5 mg once daily, taken in the morning, with or without food. In patients tolerating DAPAGLU 5 mg once daily who require additional glycemic control, the dose can be increased to 10 mg once daily. In patients with volume depletion, correcting this condition prior to initiation of DAPAGLU is recommended.

Patients with Renal Impairment

Assessment of renal function is recommended prior to initiation of DAPAGLU therapy and periodically thereafter. DAPAGLU should not be initiated in patients with an eGFR less than 60 mL/min/1.73 m2 . No dose adjustment is needed in patients with mild renal impairment (eGFR of 60 mL/min/1.73 m2 or greater). DAPAGLU should be discontinued when eGFR is persistently less than 60 mL/min/1.73 m^2.

OVERDOSAGE

There were no reports of overdose during the clinical development program for DAPAGLU. In the event of an overdose, It is reasonable to employ supportive measures, as dictated by the patient's clinical status. The removal of dapagliflozin by hemodialysis has not been studied.

STORAGE/PRECAUTIONS: Store in a cool, dry and dark place below 15-30 °C. Keep all medicines out of the reach of children. To be used on the prescription of Registered Medical Practitioners.

PRESENTATION: Dapaglu Tablets 5 & 10 mg are available in packing containing 14 tablets.

***Scotmann Specs.**

خوراک: ڈاکٹر کی ہدایت کے مطابق۔

احتیاط: روشنی، نمی اور گرمی سے بچائیں۔ 15 سے 30 ڈگری سینٹی گریڈ کے درمیان محفوظ کریں۔ تمام ادویات بچوں کی پہنچ سے دور رکھیں۔

مستند ڈاکٹر کے نسخہ پر فروخت اور استعمال کریں۔

Complete Medical Information available only for doctors on request.

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