Glysit® (Tablets)

20300
Ref. No.:B2120300/20.01

Dapagliflozin propanediol monohydrate
Sodium-glucose co-transporter 2 (SGLT2) inhibitors

GLYSIT® 5MG TABLETS (FILM COATED)
GLYSIT® 10MG TABLETS (FILM COATED)

PRESENTATION:
Glysit® 5mg Film Coated Tablets: Yellow, circular, biconvex tablet embossed C on one side and plain on the other side. Each film coated tablet contains: Dapagliflozin, Lactose and other excipients.
Glysit® 10mg Film Coated Tablets: Blue, circular, biconvex tablet embossed C on one side and plain on the other side. Each film coated tablet contains: Dapagliflozin, Lactose and other excipients.

CLINICAL PHARMACOLOGY:
The SGLT2 is selectively expressed in the kidney with no expression detected in more than 70 other tissues including liver, skeletal muscle, adipose tissue, breast, bladder and brain. SGLT2 is the predominant transporter responsible for reabsorption of glucose from the glomerular filtrate back into the circulation. Despite the presence of hyperglycaemia in type 2 diabetes, reabsorption of filtered glucose continues. Dapagliflozin improves both fasting and post-prandial plasma glucose levels by reducing renal glucose reabsorption leading to urinary glucose excretion. This glucose excretion (glucuretic effect) is observed after the first dose, is continuous over the 24-hour dosing interval and is sustained for the duration of treatment. The amount of glucose removed by the kidney through this mechanism is dependent upon the blood glucose concentration and GFR. Dapagliflozin does not impair normal endogenous glucose production in response to hypoglycaemia. Dapagliflozin acts independently of insulin secretion and insulin action.
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. Geometric mean steady-state Dapagliflozin Cmax and AUC values following once daily 10 mg doses of Dapagliflozin were 158 ng/mL and 628 ng h/mL, respectively. The absolute oral bioavailability of Dapagliflozin following the administration of a 10 mg dose is 78%. Administration with a high-fat meal decreased Dapagliflozin Cmax by up to 50% and prolonged Tmax 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, Dapagliflozin 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 litres.
Biotransformation
Dapagliflozin is extensively metabolised, primarily t =o 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. Dapagliflozin and related metabolites are primarily eliminated via urinary excretion with less than 2% as unchanged Dapagliflozin. After administration of a 50 mg [14C]-Dapagliflozin dose, 96% was recovered, 75% in urine and 21% in faeces. In faeces, approximately 15% of the dose was excreted as parent drug.

USES:
Type 2 diabetes mellitus
It is indicated in 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.
- In addition to other medicinal products for the treatment of type 2 diabetes.

Type 1 diabetes mellitus
It is indicated in adults for the treatment of insufficiently controlled type 1 diabetes mellitus as an adjunct to insulin in patients with BMI $\geq$ 27 kg/m2, when insulin alone does not provide adequate glycaemic control despite optimal insulin therapy.

DOSAGE AND ADMINISTRATION:
Type 2 Diabetes mellitus: The recommended dose is 10 mg Dapagliflozin once daily.
Type 1 Diabetes mellitus: The recommended dose is 5 mg once daily.
Dapagliflozin must only be administered as an adjunct to insulin.

CONTRA-INDICATIONS AND WARNINGS:
Hypersensitivity to the active substance or to any of the excipients.

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Adverse effects:
Contact a doctor or the nearest hospital straight away if you have any of the following side effects:
• Angioedema • Diabetic ketoacidosis • Necrotising fasciitis of the perineum or Fournier's gangrene • Loss of too much fluid from your body (dehydration) • Urinary tract infection
Very common (may affect more than 1 in 10 people)
Low blood sugar levels (hypoglycaemia)
Common • Genital infection • Back pain • Passing more water (urine) than usual or needing to pass water more often • Changes in the amount of cholesterol or fats in your blood (shown in tests) • Increases in the amount of red blood cells in your blood (shown in tests) • Decreases in creatinine renal clearance (shown in tests) in the beginning of treatment • Dizziness • Rash
Uncommon
• Thirst • Constipation • Awakening from sleep at night to pass urine • Dry mouth • Weight decreased • Increases in creatinine (shown in laboratory blood tests) in the beginning of treatment • Increases in urea (shown in laboratory blood tests)

OVERDOSAGE
Dapagliflozin did not show any toxicity in healthy subjects at single oral doses up to 500 mg (50 times the maximum recommended human dose). These subjects had detectable glucose in the urine for a dose-related period of time (at least 5 days for the 500 mg dose), with no reports of dehydration, hypotension or electrolyte imbalance, and with no clinically meaningful effect on QTc interval. The incidence of hypoglycaemia was similar to placebo. In clinical studies where once-daily doses of up to 100 mg (10 times the maximum recommended human dose) were administered for 2 weeks in healthy subjects and type 2 diabetes subjects, the incidence of hypoglycaemia was slightly higher than placebo and was not dose-related. Rates of adverse events including dehydration or hypotension were similar to placebo, and there were no clinically meaningful dose-related changes in laboratory parameters, including serum electrolytes and biomarkers of renal function.

INTERACTIONS
Diuretics
Dapagliflozin may add to the diuretaic 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. In patients with type 1 diabetes mellitus and a known risk of frequent or severe hypoglycaemia, it may be necessary to reduce the insulin dose at the time of initiating treatment with Dapagliflozin to decrease the risk of hypoglycaemia. When needed, insulin dose reduction should be done cautiously to avoid ketosis and DKA.

SPECIAL WARNINGS AND PRECAUTIONS
Renal impairment
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
Hepatic impairment
There is limited experience in clinical studies in patients with 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.
Pregnancy and Breast- Feeding
Pregnancy: There are no data from the use of dapagliflozin in pregnant women. Therefore, the use of Dapagliflozin is not recommended during the second and third trimesters of pregnancy.
Breast-feeding: It is unknown whether dapagliflozin and/or its metabolites are excreted in human milk. A risk to the newborns/infants cannot be excluded. Dapagliflozin should not be used while breast-feeding.

PHARMACEUTICAL PRECAUTIONS:
Store in a dry place below 30ºC. Protect from light. Keep all medicines out of the reach of children.

LEGAL CATEGORY: Prescription Only Medicine (POM) Regd. TM

COSMOS

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