Glem-Lin Tablets

(Empagliflozin + Linagliptin)

گلیم۔لِن ٹیبلیٹس

(ایمپاگلائی فلوزن + لینا گلپٹن)

COMPOSITION:

Glem-Lin Tablets 10mg/5mg
Each film-coated tablet contains:
Empagliflozin …….... 10mg
Linagliptin …….... 5mg
[Innovator's Specs.]

Glem-Lin Tablets 25mg/5mg
Each film-coated tablet contains:
Empagliflozin …….... 25mg
Linagliptin …….... 5mg
[Innovator's Specs.]

DESCRIPTION: Glem-Lin is a combination of Empagliflozin, a sodium-glucose co-transporter 2 (SGLT2) inhibitor and Linagliptin, a dipeptidyl peptidase-4 (DPP-4) inhibitor, indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both Empagliflozin and Linagliptin is appropriate.

INDICATIONS: Glem-Lin is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both Empagliflozin and linagliptin is appropriate. Empagliflozin is indicated to reduce the risk of cardiovascular death in adults with type 2 diabetes mellitus and established cardiovascular disease.

DOSAGE AND ADMINISTRATION: The recommended dose of **Glem-Lin** is 10mg Empagliflozin/5mg Linagliptin once daily, taken in the morning, with or without food. Dose may be increased to 25mg Empagliflozin/5mg linagliptin once daily. Assess renal function before initiating **Glem-Lin**. Do not initiate Empagliflozin + Linagliptin if eGFR is below 45ml/min/1.73 m^2. Discontinue Glem-Lin if eGFR falls persistently below 45ml/min/1.73 m^2.

CLINICAL PHARMACOLOGY: Mechanism of Action: Empagliflozin: Sodium-glucose co-transporter 2 (SGLT2) is the predominant transporter responsible for reabsorption of glucose from the glomerular filtrate back into the circulation. Empagliflozin is an inhibitor of SGLT2. By inhibiting SGLT2, Empagliflozin reduces renal reabsorption of filtered glucose and lowers the renal threshold for glucose, and thereby increases urinary glucose excretion.

Linagliptin: Linagliptin is an inhibitor of DPP-4, an enzyme that degrades the incretin hormones glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP). Thus, Linagliptin increases the concentrations of active incretin hormones, stimulating the release of insulin in a glucose-dependent manner and decreasing the levels of glucagon in the circulation.

PHARMACOKINETICS:

Absorption: Empagliflozin: The pharmacokinetics of Empagliflozin has been characterized in healthy volunteers and patients with type 2 diabetes and no clinically relevant differences were noted between the two populations. After oral administration, peak plasma concentrations of Empagliflozin were reached at 1.5 hours post-dose. Thereafter, plasma concentrations declined in a biphasic manner with a rapid distribution phase and a relatively slow terminal phase.

Linagliptin: The absolute bioavailability of Linagliptin is approximately 30%. High-fat meal reduced C_{max} by 15% and increased AUC by 4%; this effect is not clinically relevant. Linagliptin may be administered with or without food.

Distribution:

Empagliflozin: The apparent steady-state volume of distribution was estimated to be 73.8 L based on a population pharmacokinetic analysis. Following administration of an oral Empagliflozin solution to healthy subjects, the red blood cell partitioning was approximately 36.8% and plasma protein binding was 86.2%.

Linagliptin: The mean apparent volume of distribution at steady state following a single intravenous dose of Linagliptin 5mg to healthy subjects is approximately 1110L, indicating that Linagliptin extensively distributes to the tissues.

Metabolism:

Empagliflozin: No major metabolites of Empagliflozin were detected in human plasma and the most abundant metabolites were three glucuronide conjugates (2-O-, 3-O-and 6-O-glucuronide). Systemic exposure of each metabolite was less than 10% of total drug-related material.

Linagliptin: Following oral administration, the majority (about 90%) of Linagliptin is excreted unchanged, indicating that metabolism represents a minor elimination pathway.

Elimination:

Empagliflozin: The apparent terminal elimination half-life of Empagliflozin was estimated to be 12.4 h and apparent oral clearance was 10.6 L/h based on the population pharmacokinetic analysis.

Linagliptin: Following administration of an oral Linagliptin dose to healthy subjects, approximately 85% of the administered radioactivity was eliminated via the enterohepatic system (80%) or urine (5%) within 4 days of dosing. Renal clearance at steady state was approximately 70ml/min.

Rev: 09-22/0

CONTRAINDICATIONS: The combination of Empagliflozin + Linagliptin is contraindicated in patients with hypersensitivity to the active substances, to any other Sodium-Glucose-Co-Transporter-2 (SGLT2) inhibitor, to any other Dipeptidyl-Peptidase-4 (DPP-4) inhibitor, or to any of the excipients of the product.

WARNINGS AND PRECAUTIONS:
Pancreatitis: Take careful notice of potential signs and symptoms of pancreatitis. If pancreatitis is suspected, promptly discontinue Empagliflozin + Linagliptin Tablets and initiate appropriate management.
Heart Failure: Consider the risks and benefits of Empagliflozin + Linagliptin Tablets prior to initiating treatment in patients at risk for heart failure, such as those with a prior history of heart failure and a history of renal impairment, and observe these patients for signs and symptoms of heart failure during therapy.
Hypotension: Empagliflozin causes intravascular volume contraction. Symptomatic hypotension may occur after initiating Empagliflozin particularly in patients with renal impairment, the elderly, in patients with low systolic blood pressure, and in patients on diuretics.
Ketoacidosis: Reports of ketoacidosis, a serious life-threatening condition requiring urgent Patients treated with Empagliflozin + Linagliptin Tablets who present with signs and symptoms consistent with severe metabolic acidosis should be assessed for ketoacidosis regardless of presenting blood glucose levels, as ketoacidosis associated with Empagliflozin + Linagliptin Tablets may be present even if blood glucose levels are less than 250mg/dl.
Pregnancy: There are no data from the use of Empagliflozin and Linagliptin in pregnant women.
Nursing Mothers: No data in humans are available on excretion of Empagliflozin and Linagliptin into milk.

SIDE EFFECTS: The following are the side effects as described below:
- Pancreatitis.
- Heart Failure.
- Hypotension.
- Ketoacidosis.
- Acute Kidney Injury and Impairment in Renal Function.
- Urosepsis and Pyelonephritis.
- Hypoglycemia with Concomitant Use with Insulin and Insulin Secretagogues.
- Necrotizing Fasciitis of the Perineum (Fournier's Gangrene).

DRUG INTERACTIONS:
Drug Interactions with Empagliflozin:
Diuretics: Coadministration of Empagliflozin with diuretics resulted in increased urine volume and frequency of voids, which might enhance the potential for volume depletion.
Insulin or Insulin Secretagogues: Coadministration of Empagliflozin with insulin or insulin secretagogues increases the risk for hypoglycemia.
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.
Drug Interactions with Linagliptin:
Inducers of P-glycoprotein or CYP3A4 Enzymes: Rifampin decreased Linagliptin exposure, suggesting that the efficacy of Linagliptin may be reduced when administered in combination with a strong P-gp or CYP3A4 inducer. Therefore, use of alternative treatments is strongly recommended when Linagliptin is to be administered with a strong P-gp or CYP3A4 inducer.

OVERDOSE: In the event of an overdose with Empagliflozin + Linagliptin Tablets. Employ the usual supportive measures (e.g., remove unabsorbed material from the gastrointestinal tract, employ clinical monitoring, and institute supportive treatment) as dictated by the patient's clinical status.

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

PRESENTATION:
Glem-Lin Tablets 10mg/5mg are available in pack sizes of 14's.
Glem-Lin Tablets 25mg/5mg are available in pack sizes of 14'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.
17/24, Korangi Industrial Area, Karachi-Pakistan.
PHARMA
Rev: 09-22/0