Glempa

Tablets

(Empagliflozin)

گلیمپا ٹیبلیٹس

(ایمپاگلائی فلوزن)

COMPOSITION:
Glempa 10mg: Each film coated tablet contains: Empagliflozin ... 10mg.
Glempa 25mg: Each film coated tablet contains: Empagliflozin ... 25mg.
[As per Innovator's specs.]

DESCRIPTION: Glempa (Empagliflozin) Tablets contain Empagliflozin, an orally-active inhibitor of the sodium-glucose co-transporter 2 (SGLT2). The chemical name of Empagliflozin is D-Glucitol,1,5-anhydro-1-C- [4-chloro-3-[[4-[[(3S)-tetrahydro3furanyl] oxy]phenyl]methyl]phenyl]-, (1S). Its molecular formula is $C_{23}H_{27}ClO_7$.

INDICATIONS: Glempa (Empagliflozin) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus as: Monotherapy when diet and exercise alone do not provide adequate glycemic control in patients for whom use of metformin is considered inappropriate due to intolerance. - Add-on combination therapy: In combination with other glucose-lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycemic control.

DOSAGE AND ADMINISTRATION: Monotherapy and add-on combination therapy: The recommended starting dose is 10mg Empagliflozin once daily with or without food for monotherapy and add-on combination therapy with other glucose-lowering medicinal products including insulin. In patients tolerating Empagliflozin 10mg once daily who have an eGFR ≥60ml/min/1.73m² and need tighter glycemic control, the dose can be increased to 25mg once daily. The maximum daily dose is 25mg. When Empagliflozin is used in combination with a sulphonylurea or with insulin, a lower dose of the sulphonylurea or insulin may be considered to reduce the risk of hypoglycemia.
SPECIAL POPULATIONS: Renal impairment: No dose adjustment is required for patients with an eGFR ≥60ml/min/1.73m2 or CrCl ≥60ml/min. Empagliflozin should not be initiated in patients with an eGFR.
Hepatic impairment: No dose adjustment is required for patients with hepatic impairment. Empagliflozin exposure is increased in patients with severe hepatic impairment. Therapeutic experience in patients with severe hepatic impairment is limited and therefore not recommended for use in this population.
Elderly: No dose adjustment is recommended based on age. In patients 75 years and older, an increased risk for volume depletion should be taken into account. In patients aged 85 years and older, initiation of Empagliflozin therapy is not recommended due to the limited therapeutic experience.

CLINICAL PHARMACOLOGY: Mechanism of Action: 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.

PHARMACOKINETICS: Absorption: After oral administration, Empagliflozin was rapidly absorbed with peak plasma concentrations occurring at a median t_{max} of 1.5 hours post-dose. Thereafter, plasma concentrations declined in a biphasic manner with a rapid distribution phase and a relatively slow terminal phase. The steady state mean plasma AUC and C_{max} were 1870nmol.h and 259nmol/L with Empagliflozin 10mg and 4740nmol.h and 687nmol/L with Empagliflozin 25mg once daily. Systemic exposure of Empagliflozin increased in a dose-proportional manner. Administration of Empagliflozin 25mg after intake of a high-fat and high calorie meal resulted in slightly lower exposure; AUC decreased by approximately 16% and C_{max} by approximately 37% compared to fasted condition.
Distribution: The apparent steady-state volume of distribution was estimated to be 73.8L based on the population pharmacokinetic analysis. Following administration of an oral [^{14}C]-Empagliflozin solution, the red blood cell partitioning was approximately 37% and plasma protein binding was 86%.
Metabolism: No major metabolites of Empagliflozin were detected in human plasma and the most abundant metabolites were three glucuronide conjugates (2-, 3- and 6-O glucuronide). Systemic exposure of each metabolite was less than 10% of total drug-related material. The primary route of metabolism of Empagliflozin in humans is glucuronidation by the uridine 5'-diphospho-glucuronosyltransferases UGT2B7, UGT1A3, UGT1A8 and UGT1A9.
Excretion: The apparent terminal elimination half-life of Empagliflozin was estimated to be 12.4 hours and apparent oral clearance was 10.6L/hour. The inter-subject and residual variabilities for Empagliflozin oral clearance were 39.1% and 35.8%, respectively. With once-daily dosing, steady-state plasma concentrations of Empagliflozin were reached by the fifth dose. Consistent with the half-life, up to 22% accumulation, with respect to plasma AUC, was observed at steady-state. Following administration of an oral [^{14}C]-Empagliflozin solution, approximately 96% of the drug-related radioactivity was eliminated in feces (41%) or urine (54%). The majority of drug-related radioactivity recovered in feces was unchanged parent drug and approximately half of drug related radioactivity excreted in urine was unchanged parent drug.

CONTRAINDICATIONS: Empagliflozin is contraindicated in:
• Patients with known hypersensitivity to Empagliflozin or to any excipient of the product.

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• Severe renal impairment, end-stage renal disease or dialysis.

WARNINGS AND PRECAUTIONS: - 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.
- Empagliflozin increases serum creatinine and decreases eGFR. The risk of impaired renal function with Empagliflozin is increased in elderly patients and patients with moderate renal impairement.
- Insulin and insulin secretagogues are known to cause hypoglycemia. The risk of hypoglycemia is increased when Empagliflozin is used in combination with insulin secretagogues (e.g., sulphonylurea) or insulin. Therefore, a lower dose of the insulin secretagogue or insulin may be required to reduce the risk of hypoglycemia when used in combination with Empagliflozin.
- Empagliflozin increases the risk for genital mycotic infections. Patients with a history of chronic or recurrent genital mycotic infections were more likely to develop mycotic genital infections. Monitor and treat as appropriate.
- Empagliflozin increases the risk for urinary tract infections including urosepsis and pyelonephritis requiring hospitalisation in patients receiving SGLT2 inhibitors, including Empagliflozin. Monitor and treat as appropriate. Discontinuation of Empagliflozin may be considered in cases of recurrent urinary tract infections.
- Empagliflozin should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis (DKA). In patients where DKA is suspected or diagnosed, treatment with Empagliflozin should be discontinued immediately. Treatment should be interrupted in patients who are hospitalised for major surgical procedures or acute serious medical illnesses. In both cases, treatment with Empagliflozin may be restarted once the patient's condition has stabilised.
- Based on the mode of action of SGLT2 inhibitors, osmotic diuresis accompanying therapeutic glucosuria may lead to a modest decrease in blood pressure. Therefore, caution should be exercised in patients for whom an Empagliflozin induced drop in blood pressure could pose a risk, such as patients with known cardiovascular disease, patients on anti-hypertensive therapy with a history of hypotension or patients aged 75 years and older.
- Empagliflozin has minor influence on the ability to drive and use machines. Patients should be advised to take precautions to avoid hypoglycemia while driving and using machines, in particular when Empagliflozin is used in combination with a sulphonylurea and/or insulin.

PREGNANCY AND LACTATION: Pregnancy: There are no adequate and well-controlled studies of Empagliflozin in pregnant women. Empagliflozin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
Nursing Mothers: It is not known if Empagliflozin is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from Empagliflozin, a decision should be made whether to discontinue nursing or to discontinue Empagliflozin, taking into account the importance of the drug to the mother.

SIDE EFFECTS:
Very Common: Hypoglycemia (when used with sulphonylurea or insulin).
Common: Vaginal moniliasis, vulvovaginitis, balanitis and other genital infection, urinary tract infection, pruritus (generalised) and increased urination.
Uncommon: Volume depletion, dysuria and blood creatinine increased / glomerular filtration rate decreased.
Rare: Diabetic ketoacidosis.

DRUG INTERACTIONS: - Coadministration of Empagliflozin with diuretics resulted in increased urine volume and frequency of voids, which might enhance the potential for volume depletion. Empagliflozin may add to the diuretic effect of thiazide and loop diuretics and may increase the risk of dehydration and hypotension.
- Monitoring glycemic control with urine glucose tests is not recommended in patients taking SGLT2 inhibitors as it increases urinary glucose excretion and will lead to positive urine glucose tests. Use alternative methods to monitor glycemic control.
- 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.

OVERDOSE: Symptoms: Multiple daily doses of up to 100mg Empagliflozin (equivalent to 4 times the highest recommended daily dose) in patients with type 2 diabetes did not show any toxicity. Empagliflozin increased urine glucose excretion leading to an increase in urine volume.
Treatment: In the event of an overdose with Empagliflozin, 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. Removal of Empagliflozin by hemodialysis has not been studied.

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

PRESENTATION: Glempa 10mg & 25mg Tablets are available in the pack 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۔

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