EMGLIF
(Empagliflozin)

10mg, 25mg
Tablets

ایمگلِف
(ایمپاگلائیفلوزِن)

۱۰ ملی گرام
۲۵ ملی گرام
ٹیبلٹس

QUALITATIVE AND QUANTITATIVE COMPOSITION

Emglif Tablets 10mg

Each film-coated tablet contains:

Empagliflozin…..10mg

Innovator's Specs.

Emglif Tablets 25mg

Each film-coated tablet contains:

Empagliflozin…..25mg

Innovator's Specs.

DESCRIPTION

Emglif tablets contain Empagliflozin, an orally-active inhibitor of the sodium-glucose co-transporter 2 (SGLT2). Empagliflozin is a white to yellowish, non-hygroscopic powder. It is very slightly soluble in water, sparingly soluble in methanol, slightly soluble in ethanol and acetonitrile; soluble in 50% acetonitrile/water; and practically insoluble in toluene. Each film-coated tablet of Emglif contains 10mg or 25mg of Empagliflozin (free base).

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. **Pharmacodynamics:** Urinary Glucose Excretion, In patients with type 2 diabetes, urinary glucose excretion increased immediately following a dose of Emglif and was maintained at the end of a 4-week treatment period averaging at approximately 64 grams per day with 10mg Empagliflozin and 78 grams per day with 25mg Emglif once daily. **Pharmacokinetics: Absorption:** 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. The steady state mean plasma AUC and Cmax were 1870 nmol·h/L and 259 nmol/L, respectively, with 10mg Empagliflozin once daily treatment, and 4740 nmol·h/L and 687 nmol/L, respectively, with 25mg Empagliflozin once daily treatment. Systemic exposure of Empagliflozin increased in a dose-proportional manner in the therapeutic dose range. The single-dose and steady-state pharmacokinetic parameters of Empagliflozin were similar, suggesting linear pharmacokinetics with respect to time. Administration of 25mg Empagliflozin after intake of a high-fat and high-calorie meal resulted in slightly lower exposure; AUC decreased by approximately 16% and Cmax decreased by approximately 37%, compared to fasted condition. **Distribution:** 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 [14C]-Empagliflozin solution, the red blood cell partitioning was approximately 36.8% and plasma protein binding was 86.2%. **Metabolism:** 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. The primary route of metabolism of Empagliflozin in humans is glucuronidation by the uridine 5'-diphospho-glucuronosyltransferases UGT2B7, UGT1A3, UGT1A8, and UGT1A9. **Elimination:** 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. Following once-daily

dosing, up to 22% accumulation, with respect to plasma AUC, was observed at steady-state, which was consistent with Empagliflozin half-life.

INDICATIONS AND USAGE

Emglif is indicated:

•As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

•To reduce the risk of cardiovascular death in adult patients with type 2 diabetes mellitus and established cardiovascular disease.

Limitations of Use: Emglif is not recommended for patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.

CONTRAINDICATIONS

History of serious hypersensitivity reaction to Emglif. Severe renal impairment, end-stage renal disease, or dialysis.

INTERACTIONS

Diuretics: Co-administration 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: Co-administration 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.

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.

USE IN SPECIFIC POPULATION

Pregnancy: Limited data available with Emglif in pregnant women, are not sufficient to determine a drug-associated risk for major birth defects and miscarriage. There are risks to the mother and fetus associated with poorly controlled diabetes in pregnancy. **Disease associated maternal and/or embryo/fetal risk:** Poorly controlled diabetes in pregnancy increases the maternal risk for diabetic ketoacidosis, pre-eclampsia, spontaneous abortions, preterm delivery, stillbirth, and delivery complications. Poorly controlled diabetes increases the fetal risk for major birth defects, stillbirth, and macro-somia related morbidity. **Lactation:** There is no information regarding the presence of Emglif in human milk, the effects of Emglif on the breastfed infant or the effects on milk production. **Pediatric Use:** The safety and effectiveness of Emglif in pediatric patients under 18 years of age have not been established. **Geriatric Use:** 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. **Renal Impairment:** Due to the mechanism of action, the glycaemic efficacy of Empagliflozin is dependent on renal function. No dose adjustment is required for patients with an eGFR ≥60 mL/min/1.73 m2 or CrCl ≥60 mL/min. Empagliflozin should not be initiated in patients with an eGFR <60 mL/min/1.73 m2 or CrCl <60 mL/min. In patients tolerating Empagliflozin whose eGFR falls persistently below 60 mL/min/1.73 m2 or CrCl below 60 mL/min, the dose of Empagliflozin should be adjusted to or maintained at 10 mg once daily. Empagliflozin should be discontinued when eGFR is persistently below 45 mL/min/1.73 m2 or CrCl persistently below 45 mL/min. Empagliflozin should not be used in patients with end stage renal disease (ESRD) or in patients on dialysis as it is not expected to be effective in these patients. **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.

PRECAUTIONS

Hypotension: Emglif causes intravascular volume contraction. Symptomatic hypotension may occur after initiating Emglif particularly in patients with renal impairment, the elderly, in patients with low systolic blood pressure, and in patients on diuretics. Before initiating Emglif, assess for volume contraction and correct volume status if indicated. **Ketoacidosis:** Ketoacidosis, a serious life-threatening condition requiring urgent hospitalization occur in patients with type 1 and type 2 diabetes mellitus receiving sodium glucose co-transporter-2 (SGLT2) inhibitors, including Emglif. **Acute Kidney Injury and Impairment in Renal Function:** Before initiating Emglif, consider factors that may predispose patients to acute kidney injury including hypovolemia, chronic renal insufficiency, congestive heart failure and concomitant medications (diuretics, ACE inhibitors, ARBs, NSAIDs). Consider temporarily discontinuing Emglif in any setting of reduced oral intake (such as acute illness or fasting) or fluid losses (such as gastrointestinal illness or excessive heat exposure); monitor patients for signs and symptoms of acute kidney injury. If acute kidney injury occurs, discontinue Emglif promptly and institute treatment. Emglif increases serum creatinine and decreases eGFR. Patients with hypovolemia may be more susceptible to these changes. **Urosepsis and Pyelonephritis:** Serious urinary tract infections including urosepsis and pyelonephritis requiring hospitalization in patients receiving SGLT2 inhibitors, including Emglif. **Hypoglycemia with concomitant use with Insulin and Insulin Secretagogues:** Insulin and insulin secretagogues are known to cause hypoglycemia. The risk of hypoglycemia is increased when Emglif is used in combination with insulin secretagogues (e.g., sulfonylurea) 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 Emglif. **Genital Mycotic Infections:** Emglif 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. **Increased Low-Density Lipoprotein Cholesterol (LDL-C):** Increases in LDL-C can occur with Emglif. **Lactose:** The tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency, or glucose-galactose malabsorption should not take this medicinal product. **Lower limb amputations:** An increase in cases of lower limb amputation (primarily of the toe) may occur with another SGLT2 inhibitor.

ADVERSE REACTIONS

- Hypotension.
- Ketoacidosis.
- Acute Kidney Injury and Impairment in Renal Function.
- Urosepsis and Pyelonephritis.
- Hypoglycemia with Concomitant Use with Insulin and Insulin Secretagogues.
- Genital Mycotic Infections.
- Increased Low-Density Lipoprotein Cholesterol (LDL-C).

DOSAGE AND ADMINISTRATION

The recommended dose of Emglif is 10mg once daily in the morning, taken with or without food. In patients tolerating Emglif, the dose may be increased to 25mg. In patients with volume depletion, correcting this condition prior to initiation of Emglif is recommended. In patients tolerating Empagliflozin 10mg once daily who have an eGFR ≥60 mL/min/1.73 m^2 and need tighter glycaemic 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 hypoglycaemia. **Patients with Renal Impairment:** Assessment of renal function is recommended prior to initiation of Emglif and periodically thereafter. Emglif should not be initiated in patients with an eGFR less than 45 mL/min/1.73 m^2. No dose adjustment is needed in patients with an eGFR greater than or equal to 45 mL/min/1.73 m^2. Emglif should be discontinued if eGFR is less than 45 mL/min/1.73 m^2. **Overdosage:** In the event of an overdose with Emglif, employ the usual supportive measures (e.g., remove un-

absorbed material from the gastrointestinal tract, employ clinical monitoring, and institute supportive treat-ment).Removal of Empagliflozin by hemodialysis has not been studied. **Missed Dose:** Instruct patients to take Emglif only as prescribed. If a dose is missed, it should be taken as soon as the patient remembers. Advise patients not to double their next dose. The tablets can be taken with or without food, swallowed whole with water. If a dose is missed, it should be taken as soon as the patient remembers. A double dose should not be taken on the same day.

DOSAGE

As directed by the physician.

INSTRUCTIONS

Store at 25°C, excursions permitted to 15°C-30°C. Protect from sunlight and moisture. Keep all medicines out of the reach of children.

PRESENTATION

Emglif tablets 10mg are available in Alu-Alu blister pack of 2x14's.
Emglif tablets 25mg are available in Alu-Alu blister pack of 4x7's.

علامات/طریقہ استعمال

ایمگلِف ٹائپ ۲ ذیابیطس کے ان مریضوں میں علاج کے لئے تجویز کردہ ہے جو دِل کے امراض میں بھی مبتلا ہوں۔

مضر اثرات

بلڈ پریشر کا کم ہونا، کیٹو ایسیڈوسز، گردوں کی خرابی، یوروسیپسس، کولیسٹرول کا بڑھنا، جینیٹل فنگل انفیکشنز۔

احتیاطی تدابیر

بچے، حاملہ خواتین اور دودھ پلانے والی مائیں صرف ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
۷۵ سال اور اس سے زائد عمر کے مریضوں میں بلڈ پریشر کم ہونے کا خدشہ ہوسکتا ہے۔
۸۵ سال اور اُس سے زائد عمر کے مریضوں میں ایمگِلف کا استعمال ممنوع ہے۔
جگر اور گردے کے مریضوں میں ایمگِلف کا استعمال ممنوع ہے۔

خوراک: معالج کی ہدایت کے مطابق استعمال کریں۔
ہدایات: ۲۵ ڈگری سینٹی گریڈ پر رکھیں محفوظ رکھنے کی حد ۱۵ سے ۳۰ ڈگری سینٹی گریڈ ہے۔
سورج کی روشنی اور نمی سے محفوظ رکھیں۔ تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔

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