1. Name of the medicinal product:

Emjard 25 film coated Tablet
Emjard 10 film coated Tablet

2. Qualitative and quantitative composition

Emjard 10 Tablet

Each Tablet of Emjard 10 tablet contains 10 mg of Empagliflozin

Excipients with known effect

Each tablet contains lactose monohydrate

Emjard 25 Tablet

Each Tablet of Emjard 25 Tablet contains 25 mg of Empagliflozin

Excipients with known effect

Each tablet contains lactose monohydrate

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

A yellow coloured round shaped biconvex film coated tablet. Both faces are plain. Free from any visible defects

4. Clinical particulars

4.1 Therapeutic indications

Empagliflozin is indicated in:

- 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.
- Adults for the treatment of chronic kidney disease.

4.2 Posology and method of administration

Posology

The recommended dose of Emjard is 10 mg once daily, taken in the morning, with or without food. In patients tolerating Empagliflozin 10 mg, the dose may be increased to 25 mg once daily. In patients with Hypovolemia, correcting this condition prior to initiation of Empagliflozin 10 mg is recommended.

All indications

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 (see sections 4.5 and 4.8).

If a dose is missed, it should be taken as soon as the patient remembers; however, a double dose should not be taken on the same day.

Special populations

Renal impairment

Due to limited experience, it is not recommended to initiate treatment with empagliflozin in patients with an eGFR <20 ml/min/1.73 m2.

In patients with an eGFR <60 ml/min/1.73 m2 the daily dose of empagliflozin is 10 mg.

In patients with type 2 diabetes mellitus, the glucose lowering efficacy of empagliflozin is reduced in patients with an eGFR <45 ml/min/1.73 m2 and likely absent in patients with an eGFR <30 ml/min/1.73 m2. Therefore, if eGFR falls below 45 ml/min/1.73 m2, additional glucose lowering treatment should be considered if needed (see sections 4.4, 4.8, 5.1 and 5.2).

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 (see section 5.2).

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 (see sections 4.4 and 4.8).

Paediatric population

The recommended starting dose is 10 mg empagliflozin once daily. In patients tolerating empagliflozin 10 mg once daily and requiring additional glycaemic control, the dose can be increased to 25 mg once daily (see sections 5.1 and 5.2). No data are available for children with eGFR <60 ml/min/1.73 m2 and children below 10 years of age.

The safety and efficacy of empagliflozin for the treatment of heart failure or for the treatment of chronic kidney disease in children under 18 years of age have not been established. No data are available.

Method of administration

Emjard 25 Tablet is for oral use only.

Emjard 10 Tablet is for oral use only

4.3 Contraindications

Empagliflozin is contraindicated in patients with history of serious hypersensitivity reaction to Empagliflozin or any of its excipients listed in section 6.1, severe renal impairment, end-stage renal disease, or dialysis.

Empagliflozin should not be used in patients with type 1 diabetes mellitus .

4.4 Special warnings and precautions for use

General

Empagliflozin should not be used in patients with type 1 diabetes mellitus

Renal impairment
Assessment of renal function is recommended prior to initiation of Empagliflozin and periodically thereafter. Empagliflozin should not 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.

Risk for volume depletion

Based on the mode of action of SGLT2 inhibitors, osmotic diuresis accompanying glucosuria may lead to a modest decrease in blood pressure (see section 5.1). 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.

In case of conditions that may lead to fluid loss (e.g. gastrointestinal illness), careful monitoring of volume status (e.g. physical examination, blood pressure measurements, laboratory tests including haematocrit) and electrolytes is recommended for patients receiving empagliflozin. Temporary interruption of treatment with empagliflozin should be considered until the fluid loss is corrected.

Elderly

The effect of empagliflozin on urinary glucose excretion is associated with osmotic diuresis, which could affect the hydration status. Patients aged 75 years and older may be at an increased risk of volume depletion.

Complicated urinary tract infections

Cases of complicated urinary tract infections including pyelonephritis and urosepsis have been reported in patients treated with empagliflozin (see section 4.8). Temporary interruption of empagliflozin should be considered in patients with complicated urinary tract infections.

Necrotising fasciitis of the perineum (Fournier's gangrene)

Cases of necrotising fasciitis of the perineum, (also known as Fournier's gangrene), have been reported in female and male patients taking SGLT2 inhibitors, including empagliflozin. This is a rare but serious and potentially life-threatening event that requires urgent surgical intervention and antibiotic treatment.

Patients should be advised to seek medical attention if they experience a combination of symptoms of pain, tenderness, erythema, or swelling in the genital or perineal area, with fever or malaise. Be aware that either uro-genital infection or perineal abscess may precede necrotising fasciitis. If Fournier's gangrene is suspected, empagliflozin should be discontinued and prompt treatment (including antibiotics and surgical debridement) should be instituted.

Lower limb amputations

An increase in cases of lower limb amputation (primarily of the toe) has been observed in long-term clinical studies with another SGLT2 inhibitor. It is unknown whether this constitutes a class effect. Like for all diabetic patients it is important to counsel patients on routine preventative foot-care.

Hepatic injury

Cases of hepatic injury have been reported with empagliflozin in clinical trials. A causal relationship between empagliflozin and hepatic injury has not been established.

Elevated haematocrit

Haematocrit increase was observed with empagliflozin treatment (see section 4.8). Patients with pronounced elevations in haematocrit should be monitored and investigated for underlying haematological disease.

Chronic kidney disease

Patients with albuminuria may benefit more from treatment with empagliflozin.

Infiltrative disease or Takotsubo cardiomyopathy

Patients with infiltrative disease or with Takotsubo cardiomyopathy have not been specifically studied. Therefore, efficacy in these patients has not been established.

Urine laboratory assessments

Due to its mechanism of action, patients taking empagliflozin will test positive for glucose in their urine.

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

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

Lactose

The tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency, or glucose-galactose malabsorption should not take this medicinal product.

Sodium

Each tablet contains less than 1 mmol sodium (23 mg), that is to say essentially 'sodium free'.

4.5 Interaction with other medicinal products and other forms of interaction

Diuretics: Co-administration of Empagliflozin with diuretics resulted in increased urine volume. 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.

4.6 Pregnancy and Lactation

There are no adequate and well-controlled studies of Empagliflozin 10 mg in pregnant women. Empagliflozin 10 mg should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Lactation: It is not known if Empagliflozin is excreted in human milk. It is not recommended when breastfeeding.

4.7 Effects on ability to drive and use machines

Patients should be advised to take precautions to avoid hypoglycaemia while driving and using machines.

4.8 Undesirable effects

The most common adverse reactions associated with Empagliflozin are urinary tract infections and female genital mycotic infections. Others common side effects includes dehydration, hypotension, weakness, dizziness and increased thirstiness.

4.9 Overdose

In the event of an overdose with Empagliflozin the usual supportive measures (e.g., remove unabsorbed material from the gastrointestinal tract, perform clinical monitoring, and institute supportive treatment) should be employed. Removal of Empagliflozin by hemodialysis has not been studied.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drugs used in diabetes, other blood glucose lowering drugs, excl. insulins, ATC code: A10BK03 Mechanism of action: Emjard is a Sodium-glucose co-transporter 2 (SGLT2) inhibitor. 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. By inhibiting

SGLT2, Empagliflozin reduces reabsorption of filtered glucose and lowers the renal threshold for glucose (RTG), and thereby increases urinary glucose excretion. Empagliflozin improves glycemic control in patients with type 2 diabetes by reducing renal glucose reabsorption. The amount of glucose removed by the kidney through this glucuretic mechanism is dependent on blood glucose concentration and GFR. Inhibition of SGLT2 in patients with type 2 diabetes and hyperglycaemia leads to excess glucose excretion in the urine. In addition, initiation of empagliflozin increases excretion of sodium resulting in osmotic diuresis and reduced intravascular volume. In patients with type 2 diabetes, urinary glucose excretion increased immediately following the first dose of empagliflozin and is continuous over the 24 hour dosing interval. Increased urinary glucose excretion was maintained at the end of the 4-week treatment period, averaging approximately 78 g/day. Increased urinary glucose excretion resulted in an immediate reduction in plasma glucose levels in patients with type 2 diabetes.

Empagliflozin improves both fasting and post-prandial plasma glucose levels. The mechanism of action of empagliflozin is independent of beta cell function and insulin pathway and this contributes to a low risk of hypoglycaemia. Improvement of surrogate markers of beta cell function including Homeostasis Model Assessment-β (HOMA-β) was noted. In addition, urinary glucose excretion triggers calorie loss, associated with body fat loss and body weight reduction. The glucosuria observed with empagliflozin is accompanied by diuresis which may contribute to sustained and moderate reduction of blood pressure. The glucosuria, natriuresis and osmotic diuresis observed with empagliflozin may contribute to the improvement in cardiovascular outcomes. Clinical Efficacy and safety Both improvement of glycaemic control and reduction of cardiovascular morbidity and mortality are an integral part of the treatment of type 2 diabetes. Glycaemic efficacy and cardiovascular outcomes have been assessed in a total of 14,663 patients with type 2 diabetes who were treated in 12 doubleblind, placebo- and activecontrolled clinical studies, of which 9,295 received empagliflozin (empagliflozin 10 mg: 4,165 patients; empagliflozin 25 mg: 5,130 patients). Five studies had treatment durations of 24 weeks; extensions of those and other studies had patients exposed to empagliflozin for up to 102 weeks.

Treatment with empagliflozin as monotherapy and in combination with metformin, pioglitazone, a sulphonylurea, DPP-4 inhibitors, and insulin lead to clinically relevant improvements in HbA1c, fasting plasma glucose (FPG), body weight, and systolic and diastolic blood pressure. Administration of empagliflozin 25 mg resulted in a higher proportion of patients achieving HbA1c goal of less than 7% and fewer patients needing glycaemic rescue compared to empagliflozin 10 mg and placebo. Higher baseline HbA1c was associated with a greater reduction in HbA1c. In addition, empagliflozin as adjunct to standard care therapy reduced cardiovascular mortality in patients with type 2 diabetes and established cardiovascular disease.

5.2 Pharmacokinetic properties

Absorption
The pharmacokinetics of empagliflozin have been extensively characterised in healthy volunteers and patients with type 2 diabetes. After oral administration, empagliflozin was rapidly absorbed with peak plasma concentrations occurring at a median tmax 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 Cmax were 1870 nmol.h/l and 259 nmol/l with empagliflozin 10 mg and 4740 nmol.h/l and 687 nmol/l with empagliflozin 25 mg once daily. Empagliflozin 10 mg and 4740 nmol.h/l and 687 nmol/l with empagliflozin 25 mg once daily. Systemic exposure of empagliflozin increased in a dose-proportional manner. The singledose and steady-state pharmacokinetic parameters of empagliflozin were similar suggesting linear pharmacokinetics with respect to time. There were no clinically relevant differences in empagliflozin pharmacokinetics between healthy volunteers and patients with type 2 diabetes. Administration of empagliflozin 25 mg after intake of a high-fat and high calorie meal resulted in slightly lower exposure; AUC decreased by approximately 16% and Cmax by approximately 37% compared to fasted condition. The observed effect of food on empagliflozin pharmacokinetics was not considered clinically relevant and empagliflozin may be administered with or without food.

Distribution
The apparent steady-state volume of distribution was estimated to be 73.8 l based on the population pharmacokinetic analysis. Following administration of an oral [14C]-empagliflozin solution to healthy volunteers, the red blood cell partitioning was approximately 37% and plasma protein binding was 86%.

Biotransformation
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. In vitro studies suggested that the primary route of metabolism of empagliflozin in humans is glucuronidation by the uridine 5'-diphospho-glucuronosyltransferases UGT2B7, UGT1A3, UGT1A8, and UGT1A9

Elimination
Based on the population pharmacokinetic analysis, the apparent terminal elimination half-life of empagliflozin was estimated to be 12.4 hours and apparent oral clearance was 10.6 l/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 [14C]-empagliflozin solution to healthy volunteers, approximately 96% of the drug-related radioactivity was eliminated in faeces (41%) or urine (54%). The majority of drug-related radioactivity recovered in faeces was unchanged parent drug and approximately half of drug related radioactivity excreted in urine was unchanged parent drug.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, genotoxicity, fertility and early embryonic development. In long term toxicity studies in rodents and dogs, signs of toxicity were observed at exposures greater than or equal to 10-times the clinical dose of empagliflozin. Most toxicity was consistent with secondary class related to urinary glucose loss and electrolyte imbalances including decreased body weight and body fat, increased food consumption, diarrhoea, dehydration, decreased serum glucose and increases in other serum parameters reflective of increased protein metabolism and gluconeogenesis, urinary changes such as polyuria and glucosuria, and microscopic changes including mineralisation in kidney and some soft and vascular tissues. Microscopic evidence of the effects of exaggerated pharmacology on the kidney observed in some species included tubular dilatation, and tubular and pelvic mineralisation at approximately 4-times the clinical AUC exposure of empagliflozin associated with the 25 mg dose. Empagliflozin is not genotoxic

6. Pharmaceutical Particulars

6.1 List of Excipients

Lactose
Microcrystalline Cellulose (PH 101)
Croscarmellose Sodium
Hydroxypropyl Cellulose (Klucel LF)
Magnesium Stearate
Opadry Yellow 03B520024

6.2 Incompatibilities

None.

6.3 Shelf-Life

24 Months

6.4 Special Precautions for storage

Store below 30 °C, protected from moisture and light.
Store in original packaging.
Keep Out of Reach of Children**.**

6.5 Nature and Content of container

Each box contains 10's/20's/30's/50's/ 60's tablets in alu- alu blister/alu PVDC strip/HDPE bottle

6.6 Special precautions for disposal and other handling

None

7. Marketing Authorization Holder

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8. Marketing Authorization Number

CTD10996

9. Date of first authorization/renewal of the authorization

21/11/2024

10. Date of revision of the text

5/5/2025