Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product

Emjard 10 Tablet
Emjard 25 Tablet

2. Qualitative and quantitative composition

Emjard 10
Each Tablet contains 10 mg of Empagliflozin.

Emjard 25
Each Tablet contains 25 mg of Empagliflozin.

Excipients of known effect
Lactose

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Emjard 10

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

Emjard 25

A light-yellow colored 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.

4.2 Posology and method of administration

Posology

Type 2 diabetes mellitus

The recommended starting dose is 10 mg empagliflozin once daily for monotherapy and add-on combination therapy with other medicinal products for the treatment of diabetes. In patients tolerating empagliflozin 10 mg once daily who have an eGFR ≥60 ml/min/1.73 m^2 and need tighter glycaemic control, the dose can be increased to 25 mg once daily. The maximum daily dose is 25 mg (see below and section 4.4).

Heart failure

The recommended dose is 10 mg empagliflozin once daily.

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

In patients with type 2 diabetes mellitus, the glycaemic efficacy of empagliflozin is dependent on renal function. For cardiovascular risk reduction as add on to standard of care, a dose of

10 mg empagliflozin once daily should be used in patients with an eGFR below 60 ml/min/1.73 m^2 (see Table 1). Because the glycaemic lowering efficacy of empagliflozin is reduced in patients with moderate renal impairment and likely absent in patients with severe renal impairment, if further glycaemic control is needed, the addition of other anti-

hyperglycaemic agents should be considered. For dose adjustment recommendations according to eGFR or CrCL refer to Table 1.

Table 1: Dose adjustment recommendations[a]

Indication	**eGFR [ml/min/1.73 m²] or CrCL [ml/min]**	**Total daily dose**
Type 2 diabetes mellitus	≥60	Initiate with 10 mg empagliflozin. In patients tolerating 10 mg empagliflozin and requiring additional glycaemic control, the dose can be increased to 25 mg empagliflozin.
	45 to <60	Initiate with 10 mg empagliflozin.[b] Continue with 10 mg empagliflozin in patients already taking Jardiance.
	30 to <45[b]	Initiate with 10 mg empagliflozin. Continue with 10 mg empagliflozin in patients already taking Jardiance.
	<30	Empagliflozin is not recommended.
Heart or diabetes mellitus)	≥20	Recommended daily dose is 10 mg
	<20	Due to limited experience, empagliflozin is

[a] See sections 4.4, 4.8, 5.1 and 5.2

[b] patients with type 2 diabetes mellitus and established cardiovascular disease

For treatment of heart failure in patients with or without type 2 diabetes mellitus, empagliflozin 10 mg may be initiated or continued down to an eGFR of 20 ml/min/1.73 m^2 or CrCl of 20 ml/min.

Empagliflozin should not be used in patients with end stage renal disease (ESRD) or in patients on dialysis. There are insufficient data to support use in these patients (see sections 4.4, 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 safety and efficacy of empagliflozin in children and adolescents has not yet been established. No data are available.

Method of administration

The tablets can be taken with or without food, swallowed whole with water

4.3 Contraindications

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

4.4 Special warnings and precautions for use

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.

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucosegalactose malabsorption should not take this medicine.

4.5Interaction 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

Pregnancy: 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

No data available.

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.

Reporting of suspected adverse reactions: Healthcare professionals are

asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

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 glycaemic 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 double-blind, placebo- and activecontrolled clinical studies, of which 9,295 received empagliflozin (empagliflozin 10 mg: 4,165 patients; empagliflozin 10 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 10 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 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 1 870 nmol.h/l and 259 nmol/l with empagliflozin 10 mg and 4 740 nmol.h/l and 687 nmol/l with empagliflozin 25 mg once daily. Systemic exposure of empagliflozin increased in a dose-proportional manner. The single-dose 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 C_{max} 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 [^{14}C]-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 [^{14}C]-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.

Special populations

Renal impairment

In patients with mild, moderate or severe renal impairment (eGFR <30 - <90 ml/min/1.73 m^2) and patients with kidney failure/end stage renal disease (ESRD), AUC of empagliflozin increased by approximately 18%,

20%, 66%, and 48%, respectively compared to subjects with normal renal function. Peak plasma levels of empagliflozin were similar in subjects with moderate renal impairment and kidney failure/ESRD compared to patients with normal renal function. Peak plasma levels of empagliflozin were roughly 20% higher in subjects with mild and severe renal impairment as compared to subjects with normal renal function. The population pharmacokinetic analysis showed that the apparent oral clearance of empagliflozin decreased with a decrease in eGFR leading to an increase in drug exposure.

Hepatic impairment

In subjects with mild, moderate, and severe hepatic impairment according to the Child-Pugh classification, AUC of empagliflozin increased approximately by 23%, 47%, and 75% and Cmax by approximately 4%, 23%, and 48%, respectively, compared to subjects with normal hepatic function.

Body Mass Index

Body mass index had no clinically relevant effect on the pharmacokinetics of empagliflozin based on the population pharmacokinetic analysis. In this analysis, AUC was estimated to be 5.82%, 10.4%, and 17.3% lower in subjects with BMI of 30, 35, and 45 kg/m^2, respectively, compared to subjects with a body mass index of 25 kg/m^2.

Gender

Gender had no clinically relevant effect on the pharmacokinetics of empagliflozin based on the population pharmacokinetic analysis.

Race

In the population pharmacokinetic analysis, AUC was estimated to be 13.5% higher in Asians with a body mass index of 25 kg/m^2 compared to non-Asians with a body mass index of 25 kg/m^2.

Elderly

Age did not have a clinically meaningful impact on the pharmacokinetics of empagliflozin based on the population pharmacokinetic analysis.

Paediatric population

A paediatric Phase 1 study examined the pharmacokinetics and pharmacodynamics of empagliflozin (5 mg, 10 mg and 25 mg) in children and adolescents ≥10 to <18 years of age with type 2 diabetes mellitus. The observed pharmacokinetic and pharmacodynamic responses were consistent with those found in adult subjects.

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 10 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)
- Colloidal Anhydrous Silica
- Magnesium Stearate
- Opadry Yellow 03K52543 consisting of Hypromellose, Titanium Dioxide, Triacetin, Yellow Iron Oxide Non-IRR.

6.2 Incompatibilities

None.

6.3 Shelf life

24 Months

6.4 Special precautions for storage

Store below 30°C, keep away from light & moisture. Keep out of the reach of the children.

6.5 Nature and contents of container

Emjard 10 : Each box contains 20 tablets in Alu-Alu Blister pack

Emjard 25 : Each box contains 30's tablets in Alu- Alu Blister pack

6.6 Special precautions for disposal and other handling

Unused product or waste material should be disposed of in accordance with local requirements.

7. Market Authorization Holder

Square Pharmaceuticals PLC.

Square Centre

48, Mohakhali C.A, Dhaka –

1212, Bangladesh
Tel: +880 2 8833047-56, +880 2 8859007 (10 lines)
Fax: +880 2 8828768, +880 2 8834941
E-mail: info@squaregroup.com

8. Market Authorization Number
CTD10996 (Emjard 10)
CTD10999 (Emjard 25)

9. Date of First Authroization
21st Nov 2024

10. Date of Revision of the Text
11th May 2025