SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Empaflo 10 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains:

Empagliflozin……10mg

Excipients with known effect:

each tablet contains lactose monohydrate.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet (tablet). Pale yellow, biconvex, film-coated tablet plain on both sides.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Empagliflozin is indicated for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise: as monotherapy when metformin is considered inappropriate due to intolerance; and in addition to other medicinal products for the treatment of diabetes.

4.2 Posology and method of administration

The recommended starting dose is 10 mg once daily for monotherapy and add-on combination therapy. In patients tolerating 10 mg once daily who have eGFR ≥60 mL/min/1.73 m2 and need tighter glycaemic control, the dose can be increased to 25 mg once daily. Maximum daily dose is 25 mg. When used with a sulphonylurea or insulin, a lower dose of the sulphonylurea/insulin may be considered.

Renal impairment

No dose adjustment required for eGFR ≥60 mL/min/1.73 m2 or CrCl ≥60 mL/min. Should not be initiated in patients with eGFR <60 mL/min/1.73 m2 or CrCl <60 mL/min. In patients tolerating empagliflozin whose eGFR falls

below 60, the dose should be adjusted/maintained at 10 mg once daily. Discontinue when eGFR is persistently below 45 mL/min/1.73 m2 or CrCl below 45 mL/min. Not to be used in ESRD or on dialysis.

Hepatic impairment

No dose adjustment required; exposure increased in severe hepatic impairment; therapeutic experience limited, not recommended for use in this population.

Elderly

No dose adjustment recommended based on age. In patients ≥75 years, increased risk of volume depletion should be considered. Initiation not recommended in patients ≥85 years.

Paediatric population

Safety and efficacy not yet established; no data available.

Method of administration

Tablets can be taken with or without food, swallowed whole with water. If a dose is missed, take as soon as remembered; do not take a double dose on the same day.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.

4.4 Special warnings and precautions for use

Diabetic ketoacidosis

Rare cases of DKA, including life-threatening and fatal cases, have been reported with SGLT2 inhibitors including empagliflozin, sometimes with only moderately increased blood glucose (below 14 mmol/L). Treatment should be discontinued immediately if DKA is suspected/diagnosed. Interrupt treatment for major surgery/acute illness with ketone monitoring. Higher-risk patients include those with low beta-cell function reserve, restricted food intake, severe dehydration, reduced insulin doses, or increased insulin requirements. Not for use in type 1 diabetes.

Renal impairment / Monitoring of renal function

Should not be initiated below eGFR 60 mL/min/1.73 m2 or CrCl <60 mL/min; adjust/maintain at 10 mg if it falls below 60; discontinue below 45. Assess renal function prior to initiation and at least yearly, and before initiating concomitant medicines that may affect renal function.

Hepatic injury / Elevated haematocrit / Risk for volume depletion

Cases of hepatic injury reported without established causal relationship. Haematocrit increase observed. Osmotic diuresis may cause a modest decrease in blood pressure; caution in patients at risk (cardiovascular disease, anti-hypertensive therapy with history of hypotension, age ≥75). Monitor volume status/electrolytes during fluid-loss conditions; consider temporary interruption.

Elderly / Urinary tract infections / Necrotising fasciitis (Fournier's gangrene) / Lower limb amputations

Patients ≥75 years at increased risk of volume depletion; give special attention to volume intake with co-administered diuretics/ACE-inhibitors; initiation not recommended ≥85 years. UTI frequency higher with 10 mg dose; temporary interruption recommended for complicated UTIs. Rare but serious Fournier's gangrene reported; discontinue and treat promptly if suspected. Increase in lower limb amputation cases observed with another SGLT2 inhibitor; counsel on routine foot care.

Cardiac failure / Urine laboratory assessments / 1,5-AG assay interference / Lactose

Limited experience in NYHA class I-II, no experience in class III-IV. Patients will test positive for urine glucose. 1,5-AG assay unreliable for monitoring glycaemic control; use alternative methods. Contains lactose - unsuitable for rare hereditary galactose intolerance/lactase deficiency/glucose-galactose malabsorption.

4.5 Interaction with other medicinal products and other forms of interaction

Pharmacodynamic interactions

Diuretics: may add to diuretic effect of thiazide/loop diuretics, increasing dehydration/hypotension risk. Insulin/insulin secretagogues: may increase hypoglycaemia risk; lower dose may be required.

Pharmacokinetic interactions

Empagliflozin is metabolised primarily via glucuronidation (UGT1A3, UGT1A8, UGT1A9, UGT2B7) and is a substrate of OAT3, OATP1B1, OATP1B3, P-gp and BCRP (not OAT1/OCT2). Probenecid increased Cmax by 26% and AUC by 53% (not clinically meaningful). UGT induction (rifampicin, phenytoin) not recommended due to potential decreased efficacy. Gemfibrozil increased Cmax 15%/AUC 59%; rifampicin increased Cmax 75%/AUC 35% (not clinically meaningful). Verapamil (P-gp inhibitor) had no clinically relevant effect. No clinically relevant effect from metformin, glimepiride, pioglitazone, sitagliptin, linagliptin, warfarin, ramipril, simvastatin, torasemide, or hydrochlorothiazide.

Empagliflozin does not inhibit/induce CYP450 or UGT1A1/1A3/1A8/1A9/2B7 isoforms and does not inhibit P-gp at therapeutic doses; digoxin AUC increased 6% and Cmax 14% (not clinically meaningful). No clinically relevant effect on metformin, glimepiride, pioglitazone, sitagliptin, linagliptin, simvastatin, warfarin, ramipril, digoxin, diuretics or oral contraceptives.

4.6 Fertility, pregnancy and lactation

Pregnancy

No data from use in pregnant women. Animal studies show placental crossing during late gestation to a very limited extent, with no direct/indirect harm to early embryonic development, but adverse effects on postnatal development were seen. Avoid use during pregnancy as a precaution.

Breast-feeding

No human data; animal studies show excretion in milk. Should not be used during breast-feeding.

Fertility

No human fertility studies conducted; animal studies do not indicate direct/indirect harmful effects.

4.7 Effects on ability to drive and use machines

Empagliflozin has minor influence on ability to drive and use machines; caution to avoid hypoglycaemia, particularly with sulphonylurea and/or insulin combination.

4.8 Undesirable effects

A total of 15,582 patients were included in clinical safety studies; the most frequently reported adverse reaction was hypoglycaemia when used with sulphonylurea or insulin.

Common: Vaginal moniliasis, vulvovaginitis, balanitis and other genital infections; urinary tract infection (including pyelonephritis and urosepsis); thirst; pruritus (generalized); rash; increased urination; serum lipids increased; haematocrit increased. Very common: Hypoglycaemia (when used with sulphonylurea or insulin). Uncommon: Volume depletion; dysuria; urticaria; blood creatinine increased/GFR decreased. Rare: Diabetic ketoacidosis. Not known: Necrotising fasciitis of the perineum (Fournier's gangrene); angioedema.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are requested to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org'

4.9 Overdose

Symptoms

Single doses of up to 800 mg (32x max recommended dose) in healthy volunteers and multiple daily doses up to 100 mg (4x max dose) in type 2 diabetes patients did not show toxicity. Increased urine glucose excretion led to increased urine volume, which was not dose-dependent or clinically meaningful. No experience with doses above 800 mg.

Therapy

Treatment should be initiated as appropriate to clinical status. Removal by haemodialysis 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

Empagliflozin is a reversible, highly potent (IC50 1.3 nmol) and selective competitive inhibitor of SGLT2, ~5000 times more selective for SGLT2 versus SGLT1. Reduces renal glucose reabsorption leading to urinary glucose excretion; also increases sodium excretion resulting in osmotic diuresis and reduced intravascular volume.

Clinical efficacy

Assessed in 14,663 patients with type 2 diabetes across 12 double-blind studies. Monotherapy and combination therapy resulted in clinically relevant improvements in HbA1c, FPG, body weight, and blood pressure. The EMPA-REG OUTCOME study (7020 patients, median 3.1 years) demonstrated empagliflozin was superior to placebo in reducing the composite of cardiovascular death, non-fatal MI, or non-fatal stroke, driven by reduction in cardiovascular death (HR 0.62); also reduced heart failure hospitalization risk (HR 0.65) and nephropathy (HR 0.61).

5.2 Pharmacokinetic properties

Rapidly absorbed with median Tmax of 1.5 hours; steady-state mean AUC/Cmax 1870 nmol.h/L / 259 nmol/L (10 mg) and 4740 nmol.h/L / 687 nmol/L (25 mg); dose-proportional exposure. High-fat meal decreased AUC ~16% and Cmax ~37% (not clinically relevant).

Apparent Vd ~73.8 L; red blood cell partitioning ~37%; plasma protein binding 86%. Metabolised primarily by glucuronidation (UGT2B7, UGT1A3, UGT1A8, UGT1A9); no major metabolites detected. Apparent terminal half-life ~12.4 hours; apparent oral clearance 10.6 L/hour; ~96% of radioactivity eliminated in faeces (41%) or urine (54%).

Renal impairment: AUC increased ~18-66% across mild-severe impairment/ESRD. Hepatic impairment: AUC increased ~23-75% across mild-severe impairment (Child-Pugh A-C).

5.3 Preclinical safety data

No special hazard for humans based on conventional studies of safety pharmacology, genotoxicity, fertility and early embryonic development. Toxicity in long-term rodent/dog studies observed at ≥10x clinical exposure, mostly consistent with secondary pharmacology (urinary glucose loss, electrolyte imbalance). Not genotoxic. 2-year carcinogenicity studies showed tumours in male rats/mice only at high exposure multiples with mechanisms considered not relevant to humans. No adverse effects on fertility or early embryonic

development at sufficient exposure margins; not teratogenic except at maternally toxic doses (bent limb bones in rat, increased embryofetal loss in rabbit).

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

- Lactose monohydrate
- Microcrystalline cellulose
- Croscarmellose sodium
- Low-substituted hydroxypropyl cellulose
- Aerosil 200
- Magnesium stearate
- Hypromellose 6cps
- Propylene glycol
- Purified talc
- Titanium dioxide
- Yellow iron oxide
- Isopropyl alcohol
- Dichloromethane

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Alu/Alu blister packs of 3 x 10's in unit box with literature insert.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Dawa Limited,

Plot No 7879/8, Baba Dogo Road-Ruaraka,

P.O Box 16630-6200-

Nairobi-Kenya.

8. MARKETING AUTHORISATION NUMBER(S)

H2021/CTD8524/19125

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

20-09-2021

10. DATE OF REVISION OF THE TEXT

August 2020.