EMPAGLIFLOZIN PD

SCHEDULING STATUS S4

1. NAME OF THE MEDICINE

EMPAGLIFLOZIN 10 mg PD film coated tablets
EMPAGLIFLOZIN 25 mg PD film coated tablets

EMPAGLIFLOZIN PD IS CONTRAINDICATED FOR USE IN TYPE 1 DIABETES.
EMPAGLIFLOZIN PD IS NOT INDICATED FOR USE IN WEIGHT CONTROL PROGRAMMES.
There have been reports of metabolic acidosis, including ketoacidosis which were serious, life threatening or fatal, in patients taking empagliflozin. Cases of ketoacidosis have also been reported in patients without diabetes mellitus.

Patients who present with signs and symptoms including nausea, vomiting, abdominal pain, malaise and shortness of breath, should be assessed for metabolic acidosis, even if blood glucose levels are below 11 mmol/L. EMPAGLIFLOZIN PD should be discontinued, and the patient should be promptly evaluated and managed accordingly.

Predisposing factors for metabolic acidosis include insulin dose reduction, reduced caloric intake, reduced fluid intake or increased insulin requirements due to infections, illness, surgery or alcohol abuse. Caution is advised in treating these patients with EMPAGLIFLOZIN PD.

Predisposing factors for ketoacidosis include low beta-cell function reserve resulting from pancreatic disorders, e.g. history of pancreatitis or pancreatic surgery. EMPAGLIFLOZIN PD is contraindicated in these patients.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

EMPAGLIFLOZIN 10 mg PD: Each film coated tablet contains empagliflozin 10 mg.
EMPAGLIFLOZIN 25 mg PD: Each film coated tablet contains empagliflozin 25 mg.

EMPAGLIFLOZIN PD contains sugar (lactose monohydrate 45,2 mg per 10 mg tablet and 113 mg per 25 mg tablet).
Essentially 'sodium free'.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film coated tablets.
EMPAGLIFLOZIN 10 mg PD: Pale yellow, round, debossed with "L7S" on one side and the other side plain, film coated tablets.
EMPAGLIFLOZIN 25 mg PD: Pale yellow, oval, debossed with 'LU' on one side and 'E65' on the other side, film coated tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Type 2 diabetes mellitus (T2DM)
Glycaemic control:
EMPAGLIFLOZIN PD tablets are indicated as an adjunct to diet and exercise to improve glycaemic control, in adults with type 2 diabetes mellitus.

Prevention of cardiovascular events:
EMPAGLIFLOZIN PD is indicated in patients with type 2 diabetes mellitus and high cardiovascular risk* to reduce the risk of:
• cardiovascular death due to myocardial infarction
• cardiovascular death or hospitalisation for heart failure.
*e.g. previous myocardial infarction, multi vessel coronary artery disease, previous coronary revitalisation, single vessel coronary disease, at least 50 % narrowing of coronary artery lumen.

Heart failure (HF):
EMPAGLIFLOZIN PD is indicated in adult patients with heart failure (New York Heart Association (NYHA) class II-IV) independent of left ventricular ejection fraction, with or without type 2 diabetes mellitus:
• to reduce the risk of cardiovascular death and hospitalisation for heart failure
• to slow kidney function decline.

Chronic kidney disease (CKD):
EMPAGLIFLOZIN PD is indicated in adult patients with chronic kidney disease to reduce the risk of:
• kidney disease progression (sustained decline in estimated glomerular filtration rate (eGFR), end-stage kidney disease or renal death) or cardiovascular death
• all-cause hospitalisation.

4.2 Posology and method of administration

Prior to initiating therapy with EMPAGLIFLOZIN PD, hydration status and renal function should be assessed.
Do not initiate treatment if the estimated glomerular filtration rate (eGFR) < 60 mL/min/1,73 m² (or creatinine clearance < 60 mL/min) and/or in patients who are volume-depleted or acidotic (see section 4.4).

Posology
Type 2 diabetes mellitus (T2DM) indications
The recommended starting dose of EMPAGLIFLOZIN PD is 10 mg once daily.
In patients tolerating EMPAGLIFLOZIN 10 mg PD once daily, who have an eGFR ≥30 mL/min/1,73 m², and requiring additional glycaemic control, the dose may be increased to 25 mg once daily.

Heart failure (HF) indication
The recommended dose of EMPAGLIFLOZIN PD is 10 mg once daily.

Chronic kidney disease (CKD) indication
The recommended dose of EMPAGLIFLOZIN PD is 10 mg once daily.

Special populations
Patients with renal insufficiency:
Empagliflozin 10 mg can be used regardless of renal function. However, due to limited experience, it is not recommended to initiate treatment with EMPAGLIFLOZIN PD in patients on dialysis.

Glycaemic efficacy of empagliflozin is dependent on renal function and likely absent in patients with severe renal impairment. If eGFR falls below 30 mL/min/1,73 m² the recommended dose of EMPAGLIFLOZIN PD is limited to 10 mg and additional glucose lowering treatment should be considered if needed (see section 4.4).

Patients with hepatic insufficiency:
In patients with severe hepatic impairment dose adjustments may be necessary.

Elderly patients:
If the creatinine clearance is ≥ 60 mL/min, no dose adjustment based on age is recommended. Therapeutic experience in patients aged 85 years and older is limited.
Initiation of EMPAGLIFLOZIN PD therapy in this population is not recommended (see section 4.4).

Paediatric population
Safety and effectiveness of EMPAGLIFLOZIN PD in children under 18 years of age have not been established.

Method of administration
EMPAGLIFLOZIN PD should be swallowed whole, with water and can be taken with or without food.

Missed dose:
Medical practitioners should advise patients who forget to take EMPAGLIFLOZIN PD to take a dose as soon as possible and then continue with the normal dose. Patients should not take a double dose to compensate for the missed dose.

4.3 Contraindications

EMPAGLIFLOZIN PD is contraindicated in:
• hypersensitivity to empagliflozin or to any of the ingredients of EMPAGLIFLOZIN PD (see section 6.1.)
• treatment of type 1 diabetes mellitus
• treatment of ketoacidosis
• pregnancy and lactation.

4.4 Special warnings and precautions for use

EMPAGLIFLOZIN PD should not be used in patients with type 1 diabetes.

Ketoacidosis with atypical presentation:
Cases of ketoacidosis, which may be serious, life-threatening or fatal, have been reported in patients treated with empagliflozin as in EMPAGLIFLOZIN PD. Such cases require hospitalisation.
The presentation of ketoacidosis is frequently atypical with either euglycaemia or with blood glucose values mildly or moderately increased below 11 mmol/L (196 mg/dL). Although ketoacidosis is less likely to occur in patients without diabetes mellitus, cases have also been reported in these patients.
The risk of ketoacidosis must be considered in the event of non-specific symptoms such as nausea, vomiting, anorexia, abdominal pain, excessive thirst, difficulty breathing, confusion, unusual fatigue or sleepiness.
Regardless of blood glucose level, patients should be assessed for ketoacidosis immediately should these symptoms occur. Treatment with EMPAGLIFLOZIN PD is to be discontinued immediately in such cases and treatment instituted which, amongst others, may require fluids, carbohydrate and insulin.
The risk of developing ketoacidosis during therapy with EMPAGLIFLOZIN PD, is increased in patients with a reduced fluid and food intake, those on a very low carbohydrate diet, those who are severely dehydrated, insulin dose reduction in patients also requiring insulin, patients with a history of ketoacidosis or who are known to have a low beta-cell function reserve, or any pancreatic disease/disorder with or without an insulin deficiency, or in patients with alcohol abuse or misusing alcohol.
Progressive increases in blood and urine ketones as well as a progressive increase in metabolic acidosis may be indicative of the development of ketoacidosis irrespective of blood glucose levels.
Regular monitoring of blood and urine ketones as well as blood pH is recommended.
In clinical situations known to predispose to ketoacidosis (e.g. prolonged fasting due to an acute illness or surgery) the treatment with EMPAGLIFLOZIN PD should be temporarily discontinued.
In these situations, consider monitoring of ketones, even if EMPAGLIFLOZIN PD treatment has been interrupted.
Treatment should be interrupted in patients who are hospitalised for acute serious medical illnesses.
The underlying mechanism for sodium-glucose co-transporter 2 (SGLT2) inhibition-associated ketoacidosis has not been established.
Atypical metabolic acidosis (no ketone bodies) may present in a very similar manner to ketoacidosis.

Haemoconcentration:
An increase in the haematocrit of patients on EMPAGLIFLOZIN PD therapy is to be expected.

Use in patients with renal impairment:
As the efficacy of EMPAGLIFLOZIN PD is dependent on renal function, assessment of renal function is recommended prior to EMPAGLIFLOZIN PD initiation and periodically during treatment, i.e. at least 6-monthly.
EMPAGLIFLOZIN PD 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 4.2, 5.1 and 5.2). Glycaemic efficacy of EMPAGLIFLOZIN PD is dependent on renal function and likely absent in patients with an eGFR<30 mL/min/1,73 m² (see section 4.2).

Monitoring of renal function:
Assessment of renal function is recommended prior to EMPAGLIFLOZIN PD initiation and periodically during treatment, i.e. at least 6-monthly.

Hepatic injury:
Cases of hepatic injury have been reported during empagliflozin therapy.

Use in patients at risk for volume depletion:
Based on the mode of action of SGLT2 inhibitors, osmotic diuresis accompanying therapeutic glycosuria may lead to intravascular volume contraction with a 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 antihypertensive therapy and/or diuretics, and with a history of hypotension, or the elderly especially patients aged 75 years and older.
Should conditions that may lead to fluid loss, such as gastrointestinal illness, arise, careful monitoring of volume status (e.g. physical examination, blood pressure measurements, laboratory tests including haematocrit) and electrolytes is recommended for patients receiving EMPAGLIFLOZIN PD. Temporary interruption of treatment with EMPAGLIFLOZIN PD should be considered until the fluid loss is corrected.

Urinary tract infections and genital infections:
Studies show that patients treated with empagliflozin showed an overall increase in frequency of urinary tract infection, and/or genital infection than those treated with placebo (see section 4.8), especially mycotic infections in females. Genital infections occurred more frequently in females than in males. Balanoposthitis in males may result in phimosis.

Urosepsis and pyelonephritis:
Patients with a history of chronic or recurrent urinary tract infection (UTI) were more likely to experience UTI.
Cases of complicated urinary tract infections including pyelonephritis and urosepsis have been reported in patients treated with EMPAGLIFLOZIN PD (see section 4.8).
Temporary interruption of EMPAGLIFLOZIN PD should be considered in patients with complicated urinary tract infections.

Heart failure:
EMPAGLIFLOZIN PD is not recommended in patients with eGFR <20 mL/min/1,73 m².

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 with diabetes mellitus taking SGLT2 inhibitors.
This is a rare but serious and potentially life-threatening event that requires urgent surgical intervention and antibiotic treatment.
Serious outcomes have included hospitalisation, multiple surgeries, and death.
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 PD 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.

Urine laboratory assessments:
Due to the mechanism of action, patients taking EMPAGLIFLOZIN PD 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.

Additional information on special populations:
Elderly patients:
Elderly patients (aged 75 years and older) are at increased risk of volume depletion.
EMPAGLIFLOZIN PD should therefore be prescribed with caution in these patients (see section 4.8).
Therapeutic experience in patients aged 85 years and older is limited. Initiation of EMPAGLIFLOZIN PD therapy in this population is not recommended.

Excipients:
EMPAGLIFLOZIN PD contains lactose. Patients with the rare hereditary conditions of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take EMPAGLIFLOZIN PD.

EMPAGLIFLOZIN PD contains less than 1 mmol sodium (0,023 g) per dose, that is to say essentially 'sodium-free'.

Paediatric population
EMPAGLIFLOZIN PD is not recommended for use in children below 18 years due to lack of data on safety and efficacy.

4.5 Interaction with other medicines and other forms of interaction

Effects on laboratory tests: Interference with 1,5-anhydroglucitol (1,5-AG) Assay:
Monitoring of glycaemic control cannot be done by urine glucose monitoring or with a 1,5 AG blood assay, as SGLT2 inhibitors interfere with the assay.

Lithium:
Concomitant use of SGLT2 inhibitors, including empagliflozin, with lithium may decrease blood lithium levels through increased renal lithium elimination. Therefore, serum lithium concentration should be monitored more frequently with empagliflozin initiation or following dose changes. Please refer the patient to the lithium prescribing medical practitioner in order to monitor serum concentration of lithium.

Effects of EMPAGLIFLOZIN PD on other medicines
***In vitro* assessment of medicine interactions:**
EMPAGLIFLOZIN PD does not inhibit, inactivate, or induce CYP450 isoforms.

4.6 Fertility, pregnancy and lactation

EMPAGLIFLOZIN PD is contraindicated in pregnancy and lactation (see section 4.3).

Pregnancy
Animal studies showed that empagliflozin as contained in EMPAGLIFLOZIN PD crosses the placenta.

Breastfeeding
EMPAGLIFLOZIN PD is contraindicated when breastfeeding (see section 4.3).
Animal studies have shown excretion of empagliflozin in milk of animals, therefore a risk to human newborns/infants cannot be excluded.

Fertility
There is no data on fertility with EMPAGLIFLOZIN PD.

4.7 Effects on ability to drive and use machines

EMPAGLIFLOZIN PD is expected to have influence on the ability to drive and use machines. Hypoglycaemia may impair driving and machinery use capabilities. Patients should be advised to avoid the onset of hypoglycaemia, and act appropriately.

4.8 Undesirable effects

SIDE EFFECTS:
a). Summary of the safety profile
Type 2 diabetes:
Patients with type 2 diabetes were treated in clinical studies to evaluate the safety of empagliflozin (as in EMPAGLIFLOZIN PD), of which 64 % of the patients were treated with empagliflozin. In further clinical trials, some patients received treatment with empagliflozin 10 mg and others received treatment with empagliflozin 25 mg for periods of at least 24 weeks and at least 76 weeks.
In these trials, the frequency of adverse effects leading to discontinuation was similar in all treatment groups: for placebo (5,3 %), empagliflozin 10 mg (4,8 %) and empagliflozin 25 mg (4,9 %).
The most frequent adverse effect reported was hypoglycaemia, which depended on the type of background therapy used in the respective studies.

Heart failure:
The EMPEROR-Reduced study included 3730 patients with heart failure and reduced ejection fraction treated with empagliflozin 10 mg (as in EMPAGLIFLOZIN PD) or placebo.
Approximately half of the patients had type 2 diabetes mellitus. The most frequent adverse reaction was volume depletion (empagliflozin 10 mg: 10,6%, placebo: 9.9%). Major hypoglycaemia (events requiring assistance) was observed only in patients with diabetes mellitus.
No new adverse reactions were identified in the EMPEROR-Reduced heart failure study.

Chronic kidney disease indication:
The EMPA-KIDNEY study included patients with chronic kidney disease (N = 6 609) treated with 10 mg empagliflozin or placebo. About 44 % of the patients had type 2 diabetes mellitus.
No new adverse reactions were identified in the EMPA-KIDNEY study.
The overall safety profile of empagliflozin was generally consistent across the studied indications.

b). Tabulated summary of adverse reactions
The frequencies of adverse events are ranked according to the following:
Frequent = (≥ 1/100 to < 1/10).
Less frequent = Infrequent (≥ 1/1,000 to < 1/100); Rare (≥ 1/10,000 to < 1/1,000); Very rare (<1/10,000).
Frequency not known = cannot be estimated from the available data.

System organ class	Frequency	Side effects
Infections and infestations	*Frequent*	Vaginal moniliasis, vulvovaginitis, balanitis and other genital infections, urinary tract infection (including urosepsis and pyelonephritis)
	Less frequent	Necrotising fasciitis of the perineum (Fournier's gangrene) in in heart failure
	Frequency unknown	Necrotising fasciitis of the perineum (Fournier's gangrene) in T2DM
Metabolism and nutrition disorders	*Frequent*	Weight loss, serum lipids increased
	Frequency unknown	Diabetic ketoacidosis
Vascular disorders	*Frequent*	Volume depletion (hypotension and dehydration)
	Less frequent	Volume depletion (hypotension and dehydration) in T2DM
Gastrointestinal disorders	*Frequent*	Thirst (10 mg, 25 mg tablet) , constipation (10 mg tablet) in T2DM
	Less Frequent	Constipation (25 mg tablet) in T2DM, thirst in heart failure
Skin and subcutaneous tissue disorders	*Frequent*	Pruritus, rash
	Less frequent	Urticaria, angioedema
Renal and urinary disorders	*Frequent*	Glycosuria, increased urination in T2DM
	Less frequent	Glycosuria and increased urination in heart failure, dysuria, ketonuria, fluid volume depletion/dehydration, increased blood creatinine, decreased GFR (glomerular filtration rate) in T2DM and heart failure
Reproductive system and breast disorders	*Frequency unknown*	Phimosis*
Investigations	*Less Frequent*	Increased haematocrit (haemoconcentration)

*Post marketing experience.

c). Description of selected adverse reactions
Volume depletion:
The overall frequency of volume depletion (including the predefined terms blood pressure (ambulatory) decreased, blood pressure systolic decreased, dehydration, hypotension, hypovolaemia, orthostatic hypotension and syncope) of empagliflozin (as in EMPAGLIFLOZIN PD) was similar to placebo (empagliflozin 10 mg - 0.5 %, empagliflozin 25 mg - 0.3 % and placebo - 0.3 %). The effect of empagliflozin on urinary glucose excretion is associated with osmotic diuresis, which could affect hydration status of patients age 75 years and older or those otherwise at risk. In patients 75 ≥ years of age the frequency of volume depletion events was similar for empagliflozin 10 mg (2,3 %) compared to placebo (2,1 %), but it increased with empagliflozin 25 mg (4,4 %).

Blood creatinine increased and glomerular filtration rate decreased:
The overall frequency of patients with increased blood creatinine and decreased glomerular filtration rate was similar between empagliflozin and placebo. In placebo controlled, double-blind studies up to 76 weeks, initial transient increases in creatinine and initial transient decreases in estimated glomerular filtration rates have been observed. These changes were generally reversible during continuous treatment or after medicine discontinuation.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety 2 SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.
An email can be sent directly to the company, pharmacovigilance@pharmadynamics.co.za, to ensure safety of the product.

4.9 Overdose

Signs and symptoms:
The risk and severity of side effects may be increased (see section 4.8).

Management of overdose:
In the event of an overdose, symptomatic and supportive treatment should be initiated as appropriate to the patient's clinical status. The removal of empagliflozin by haemodialysis has not been studied.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drugs used in diabetes, sodium-glucose co-transporter 2 (SGLT2) inhibitors
ATC code: A10BK03
Pharmacological classification: A 21.2 Oral hypoglycaemics

Mechanism of action
Empagliflozin is a reversible inhibitor of SGLT2 (sodium-glucose co-transporter 2) with an IC50 of 1,3 nM. It has a 5 000-fold selectivity over human SGLT1 (IC50 of 6 278 nM), responsible for glucose absorption in the gut. Furthermore, high selectivity could be shown toward other glucose transporters (GLUTs) responsible for glucose homeostasis in the different tissues.
SGLT2 is highly expressed in the kidney, whereas expression in other tissues is absent or very low. It is responsible as the predominant transporter for reabsorption of glucose from the glomerular filtrate back into the circulation. In patients with type 2 diabetes mellitus (T2DM) and hyperglycaemia a higher amount of glucose is filtered and reabsorbed.
Empagliflozin improves glycaemic control in patients with type 2 diabetes mellitus by reducing renal glucose reabsorption. The amount of glucose removed by the kidney through this glycuretic mechanism is dependent upon the blood glucose concentration and GFR.
Through inhibition of SGLT2 in patients with T2DM and hyperglycaemia, excess glucose is excreted in the urine.
The effect of empagliflozin in lowering blood glucose is independent of beta-cell function and insulin pathway. Urinary glucose excretion triggers caloric loss, associated with body fat loss and body weight reduction.
The glycosuria observed with empagliflozin is accompanied by mild diuresis which may contribute to sustained and moderate reduction of blood pressure.
Empagliflozin also reduces sodium reabsorption and increases the delivery of sodium to the distal tubule. This may influence several physiological functions including, but not restricted to: increasing tubuloglomerular feedback and reducing intraglomerular pressure, lowering both pre- and afterload of the heart, downregulating sympathetic activity and reducing left ventricular wall stress as evidenced by lower NT-proBNP values which may have beneficial effects on cardiac remodelling, filling pressures and diastolic function as well as preserving kidney structure and function. Other effects such as an increase in haematocrit, a reduction in body weight and blood pressure may further contribute to the beneficial cardiac and renal effects.

5.2 Pharmacokinetic properties

Absorption:
The pharmacokinetics of empagliflozin have been extensively characterised in healthy volunteers and patients with T2DM. After oral administration, empagliflozin was absorbed with peak plasma concentrations occurring at a median t_{max} 1,5 h post-dose.
Thereafter, plasma concentrations declined in a biphasic manner with a rapid distribution phase and a relatively slow terminal phase. For single doses of 10 mg and 25 mg, the terminal phase half-life is 13,1 ± 4,0 h and 10,2 ± 2,1 h, respectively. The steady-state mean plasma AUC was 4 740 nmol.h/L and C_{max} was 687 nmol/L with 25 mg empagliflozin once daily (qd). Systemic exposure of empagliflozin increased in a dose-proportional manner. The single-dose and steady-state pharmacokinetics 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 mellitus.

Administration of 25 mg empagliflozin after intake of a high-fat and high calorie meal resulted in slightly lower exposure; AUC decreased by approximately 16 % and C_{max} decreased 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 a population pharmacokinetic analysis.
Following administration of an oral [^{14}C]-empagliflozin solution to healthy participants, the red blood cell partitioning was approximately 36,8 % and plasma protein binding was 86,2 %.

Biotransformation:
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.
In vitro studies suggested that the primary route of metabolism of empagliflozin in humans is glucuronidation by the uridine 5'-diphosphoglucuronosyltransferases 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. 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 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 participants, approximately 95,6 % of the medicine related radioactivity was eliminated in faeces (41,2 %) or urine (54,4 %). The majority of medicine related radioactivity recovered in faeces was unchanged parent medicine and approximately half of medicine related radioactivity excreted in urine was unchanged parent medicine.

Pharmacokinetics in special patient groups:
Renal insufficiency:
In patients with mild (eGFR: 60 - < 90 mL/min/1,73 m2), moderate (eGFR: 30 - < 60 mL/min/1,73 m²), renal impairment and severe (eGFR: < 30 mL/min/1,73 m²) patients with kidney failure/ESRD (end stage renal disease) patients, AUC of empagliflozin increased by approximately 18 %, 20 %, 66 %, and 48 %, respectively, compared to patients with normal renal function.

Hepatic insufficiency:
In patients with mild, moderate, and severe hepatic impairment according to the Child-Pugh classification, AUC of empagliflozin increased approximately by 23 %, 47 %, and 75 % and C_{max} by approximately 4 %, 23 %, and 48 %, respectively, compared to patients with normal hepatic function. Based on pharmacokinetics, dosage adjustment may be necessary in patients with severe hepatic impairment.

Body mass index (BMI):
No dosage adjustment is necessary based on BMI. Body mass index had no clinically relevant effect on the pharmacokinetics of empagliflozin based on the population pharmacokinetic analysis.

Gender:
No dosage adjustment is necessary based on gender.

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

Paediatric population
Studies characterising the pharmacokinetics of empagliflozin in paediatric patients have not been performed.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet cores:
Croscarmellose sodium
Colloidal silicon dioxide
Hydroxypropyl cellulose
Lactose monohydrate
Magnesium stearate
Microcrystalline cellulose.

Film coating: (Opadry Yellow)
HPMC (hypromellose)
Iron Oxide Yellow
Macrogol/PEG
Titanium Dioxide

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 25 °C. Keep container well closed. Protect from light and moisture.

6.5 Nature and contents of container

EMPAGLIFLOZIN 10 mg PD:
30, 60 and 90 tablets: 50 mL round opaque white, 33 mm neck HDPE bottles, with a child resistant cap and printed heat-seal liner, containing 30, 60 or 90 tablets, packed in a printed outer carton.
500 tablets: 60 mL round opaque white, 33 mm neck HDPE bottles, with a child resistant cap and printed heat-seal liner, containing 500 tablets.
Not all pack sizes are marketed.

EMPAGLIFLOZIN 25 mg PD:
30, 60 and 90 tablets: 50 mL round opaque white, 33 mm neck HDPE bottles, with a child resistant cap and printed heat-seal liner, containing 30, 60 or 90 tablets, packed in a printed outer carton.
500 tablets: 150 mL round opaque white, 38 mm neck HDPE bottles, with a child resistant cap and printed heat-seal liner, containing 500 tablets.
Not all pack sizes are marketed.

6.6 Special precautions for disposal

No special precautions.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION

Pharma Dynamics (Pty) Ltd
1st Floor Grapevine House, Steenberg Office Park
Silverwood Close
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Tel.: +27 21 707 7000
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8. REGISTRATION NUMBERS

EMPAGLIFLOZIN 10 mg PD: A56/21.2/0973
EMPAGLIFLOZIN 25 mg PD: A56/21.2/0974

9. DATE OF FIRST AUTHORISATION

15 April 2025

10. DATE OF REVISION OF THE TEXT

May 2026

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS S4

EMPAGLIFLOZIN 10 mg PD film coated tablets
EMPAGLIFLOZIN 25 mg PD film coated tablets
Empagliflozin
EMPAGLIFLOZIN PD contains sugar (lactose monohydrate)
45,2 mg per 10 mg tablet and 113 mg per 25 mg tablet.
Essentially 'sodium free'.

Read all of this leaflet carefully before you start taking EMPAGLIFLOZIN PD
- Keep this leaflet. You may need to read it again
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider
- EMPAGLIFLOZIN PD has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

Do not take EMPAGLIFLOZIN PD if you have type 1 diabetes, EMPAGLIFLOZIN PD is used together with diet and exercise to lower blood sugar in adults with type 2 diabetes only. EMPAGLIFLOZIN PD is not used to control body weight.

There have been reports of metabolic acidosis, including ketoacidosis (a serious complication of diabetes) which were serious, life threatening or fatal, in patients taking EMPAGLIFLOZIN PD.

If you have any symptoms of metabolic acidosis such as feeling sick or being sick, stomach pain, excessive thirst, fast and deep breathing, confusion, unusual sleepiness or tiredness, a sweet smell to your breath, a sweet or metallic taste in your mouth, or a different odour to your urine or sweat, you must immediately contact a doctor or the nearest hospital in order to be assessed for metabolic acidosis, even if your blood glucose level is below 11 mmol/L. Please refer also to 'Warnings and precautions'.

What is in this leaflet

1. What EMPAGLIFLOZIN PD is and what it is used for
EMPAGLIFLOZIN PD contains the active substance empagliflozin.
EMPAGLIFLOZIN PD is a member of a group of medicines called sodium-glucose co-transporter 2 (SGLT2) inhibitors.

EMPAGLIFLOZIN PD works by blocking the SGLT2 protein in your kidneys. This causes blood sugar (glucose) to be removed in your urine, thereby lowering the amount of sugar in your blood.
It is important that you continue with your diet and exercise plan as told to you by your health provider.

Type 2 diabetes mellitus
- EMPAGLIFLOZIN PD is used to treat type 2 diabetes in adult patients (aged 18 years and older) that cannot be controlled by diet and exercise alone.

What is type 2 diabetes?
Type 2 diabetes is a disease that comes from both your genes and your lifestyle. If you have type 2 diabetes, your pancreas does not make enough insulin to control the level of glucose in your blood, and your body is unable to use its own insulin effectively. This results in high levels of glucose in your blood which can lead to medical problems like heart disease, kidney disease, blindness, and poor circulation in your limbs.

Prevention of cardiovascular events
EMPAGLIFLOZIN PD is also used in adults with 'type 2 diabetes' with an increased cardiovascular risk (health problems due to your heart and blood vessels), to lower the risk of dying from a heart attack or other events related to your heart or blood vessels, or to reduce the risk of being admitted to hospital for heart failure.

Heart failure
EMPAGLIFLOZIN PD is used to treat heart failure in adults with or without type 2 diabetes, to reduce the risk of cardiovascular death and to reduce hospitalisation for heart failure. EMPAGLIFLOZIN PD also helps to slow down the worsening of kidney function.

Heart failure occurs when your heart is too weak or stiff and cannot work properly. This can lead to serious medical problems and need for hospital care. The most common symptoms of heart failure are feeling breathless, feeling tired or very tired all the time and ankle swelling.

EMPAGLIFLOZIN PD helps protect your heart from getting weaker and improves your symptoms.

Chronic kidney disease
EMPAGLIFLOZIN PD is used in adults with chronic kidney disease to reduce the risk of:
- progression of your kidney disease or death due to problems with your heart or blood vessels
- hospitalisation from any cause.

Chronic kidney disease is a long-term condition. It might be caused by other diseases such as diabetes and high blood pressure or even by your own immune system attacking the kidneys. When you have chronic kidney disease, your kidneys may gradually lose their ability to clean and filter your blood properly. This can lead to serious medical problems such as swollen legs, heart failure or need for hospital care. EMPAGLIFLOZIN PD helps protect your kidneys from losing their function.

2. What you need to know before you take EMPAGLIFLOZIN PD
Do not take EMPAGLIFLOZIN PD:
- if you are hypersensitive (allergic) to empagliflozin or any of the other ingredients of EMPAGLIFLOZIN PD (see section 6)
- if you have type 1 diabetes mellitus (a chronic condition in which the pancreas produces little or no insulin)
- if you have been diagnosed with ketoacidosis (a serious complication of diabetes that occurs when your body produces high levels of blood acids called ketones)
- if you are pregnant or breastfeeding your baby.

Warnings and precautions
Take special care with EMPAGLIFLOZIN PD:
- if you have type 1 diabetes (your body does not produce any insulin). EMPAGLIFLOZIN PD should not be used to treat type 1 diabetes
- if you experience rapid weight loss, feeling sick or being sick, stomach pain, excessive thirst, fast and deep breathing, confusion, unusual sleepiness or tiredness, a sweet smell to your breath, a sweet or metallic taste in your mouth, or a different odour to your urine or sweat, contact a doctor or the nearest hospital straight away. These symptoms could be a sign of "ketoacidosis" - a rare, but serious, sometimes life-threatening problem that occurs when your body produces high levels of blood acids called ketones in your urine or blood, as seen in blood tests.
  The risk of developing ketoacidosis may be increased with prolonged fasting, excessive alcohol consumption, dehydration, sudden reductions in insulin dose, or a higher need of insulin due to major surgery or serious illness
- if you have an increase in the volume percentage of red blood cells in blood, measured as part of a blood test
- if you have serious kidney problems or are on renal dialysis. Your medical practitioner may limit your dose to 10 mg once a day or ask you to take a different medicine (see also section 3, 'How to take EMPAGLIFLOZIN PD). Your kidney function should be assessed before you start taking EMPAGLIFLOZIN PD, at least 6-monthly during treatment
- if you have liver problems
- if you are at increased risk of low blood pressure, such as patients with heart disease, have a history of low blood pressure, are taking medicines to treat high blood pressure or are 75 years old or older, as increased passing of urine due to the medicine may affect fluid balance in your body and increase your risk of dehydration
- if you have been vomiting, have diarrhoea or fever, or if you are not able to eat or drink. These conditions can cause dehydration. Your doctor may ask you to stop taking EMPAGLIFLOZIN PD until you recover, to prevent loss of too much body fluid
- if you have a serious infection of the kidney or the urinary tract, with fever. Your doctor may ask you to stop taking EMPAGLIFLOZIN PD until you have recovered
- if you have been diagnosed with heart failure (a chronic condition in which the heart doesn't pump blood as well as it should)
- talk to your medical practitioner immediately if you:
  - develop a combination of symptoms of pain, tenderness, redness, or swelling of the genitals or the area between the genitals and the anus with fever or feeling generally unwell, immediately inform your doctor. These symptoms could be a sign of a rare but serious or even life-threatening infection, called necrotising fasciitis of the perineum or Fournier's gangrene which destroys the tissue under the skin. Fournier's gangrene has to be treated immediately
  - have symptoms of genital burning, redness, pain and discharge which may be signs of a genital infection
- like for all diabetic patients it is important to check your feet regularly and adhere to any other advice regarding foot care given by your healthcare professional
- because of how this medicine works, your urine will test positive for sugar while you are taking EMPAGLIFLOZIN PD
- if you are 75 years old or older as starting this medicine above 75 years is not recommended.

Children and adolescents
EMPAGLIFLOZIN PD is not recommended for children and adolescents under 18 years, because it has not been studied in these patients.

Other medicines and EMPAGLIFLOZIN PD
Always tell your healthcare provider if you are taking any other medicine. (This includes complementary or traditional medicines.)
- if you are taking lithium (a mood stabilizing medicine used to treat certain mental illnesses). EMPAGLIFLOZIN PD can lower the amount of lithium in your blood.

EMPAGLIFLOZIN PD with food and drink
EMPAGLIFLOZIN PD can be taken with or without food.

Pregnancy, breastfeeding and fertility
If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before using EMPAGLIFLOZIN PD.
Do not use EMPAGLIFLOZIN PD if you are pregnant. It is unknown if EMPAGLIFLOZIN PD is harmful to the unborn child. Do not use EMPAGLIFLOZIN PD if you are breastfeeding. It is not known if EMPAGLIFLOZIN PD passes into human breast milk.

Driving and using machines:
EMPAGLIFLOZIN PD may influence the ability to drive and use machines. If you experience symptoms of low blood sugar such as shaking, sweating, anxiety, blurred vision, tingling lips, paleness, mood change or confusion while taking EMPAGLIFLOZIN PD do not drive or use machines and contact your healthcare provider immediately.
It is not always possible to predict to what extent EMPAGLIFLOZIN PD may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which EMPAGLIFLOZIN PD affects them.

EMPAGLIFLOZIN PD contains:
Lactose
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

Sodium
EMPAGLIFLOZIN PD contains less than 1 mmol sodium (0,023 g) per dose, that is to say essentially 'sodium-free'.

3. How to take EMPAGLIFLOZIN PD
Do not share medicines prescribed for you with any other person. Always use EMPAGLIFLOZIN PD exactly as your doctor has instructed. You should check with your doctor or pharmacist if you are unsure.

Swallow the tablet whole with water. You can take the tablet with or without food.

Type 2 Diabetes
The usual dose of EMPAGLIFLOZIN PD is one 10 mg tablet once a day. Your doctor will decide whether to increase your dose to 25 mg once a day, if needed to help to control your blood sugar. Check your blood sugar as your healthcare professional advises you to. Appropriate diet and exercise can help your body use its blood sugar better. It is important to stay on the diet and exercise progam recommended by your healthcare provider while taking EMPAGLIFLOZIN PD.

Heart failure or chronic kidney disease
The usual dose of EMPAGLIFLOZIN PD is one 10 mg tablet once a day.

Kidney disease:
Talk to your doctor if you have kidney problems. Your doctor may limit your dose or decide to use an alternative medicine.

Liver problems:
Talk to your doctor in case you suffer from severe liver disease as your doctor may need to adjust your dose of EMPAGLIFLOZIN PD.

Elderly:
There is very little experience in patients aged 85 years or older. Treatment with EMPAGLIFLOZIN PD should not be started in patients above the age of 85.

Remember to take all medicines as directed by your doctor to achieve the best results for your health.
Diet and exercise can help your body to use its blood sugar better. It is important to stay on the diet and exercise program recommended by your doctor during treatment with this medicine.

Your doctor will tell you how long your treatment with EMPAGLIFLOZIN PD will last. Do not stop treatment early because your blood sugar levels may increase.

If you have the impression that the effect of EMPAGLIFLOZIN PD is too strong or too weak, tell your doctor or pharmacist.

If you take more EMPAGLIFLOZIN PD than you should:
In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

Symptoms of overdose may include:
- increased risk and severity of side effects as listed in section 4.

If you forget to take EMPAGLIFLOZIN PD:
If you forget to take EMPAGLIFLOZIN PD, take as soon as you remember on the same day. If you do not take a tablet that same day, take your normal dose the next day. Do not take a double dose to make up for forgotten individual doses.

If you stop taking EMPAGLIFLOZIN PD:
Do not stop taking EMPAGLIFLOZIN PD without first consulting your doctor. If you have type 2 diabetes mellitus, your blood sugar levels may increase when you stop taking EMPAGLIFLOZIN PD.
If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects
EMPAGLIFLOZIN PD can have side effects.
Not all side effects reported for EMPAGLIFLOZIN PD are included in this leaflet.
Should your general health worsen, or if you experience any untoward effects while using EMPAGLIFLOZIN PD, please consult your healthcare provider for advice.

If any of the following happens, stop using EMPAGLIFLOZIN PD and tell your doctor immediately or go to the casualty department at your nearest hospital:
- swelling of the face, lips, mouth, tongue, or throat that may lead to difficulty breathing or swallowing
- rash or itching
- fainting.

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to EMPAGLIFLOZIN PD. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:
- diabetic ketoacidosis (symptoms include: rapid weight loss, nausea and vomiting, stomach pain excessive thirst, rapid and deep breathing, confusion, unusual sleepiness or tiredness, a sweet smell to your breath, a sweet or metallic taste in your mouth or a different odour to your urine or sweat)
- pain or tenderness, itching, swelling in the genital or back passage area, fever or are generally feeling unwell. These may be symptoms of a serious and life threatening infection called Fournier's gangrene
- have symptoms of genital burning, redness, pain and discharge which may be signs of a genital infection.

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:
Frequent side effects:
- genital yeast infection like thrush, inflamed nose or throat, (nasopharyngitis), cough
- sepsis caused by a urogenital tract infection (urosepsis), inflammation of the kidney as a result of bacterial infection (pyelonephritis)
- low blood sugar (hypoglycaemia) when taken with other antidiabetic medicines, with symptoms that include shaking, sweating, feeling very anxious or confused, fast heartbeat, excessive hunger, headache
- weight loss, high cholesterol levels in your blood
- excess of sugar in the urine, increased urination
- rash, itching
- thirst
- constipation.

Less frequent side effects:
- dehydration (with symptoms that may include unusual thirst, light-headedness or dizziness upon standing, fainting or loss of consciousness), low blood pressure
- hives (reddened, itchy welts), swelling of the area beneath the skin or mouth
- pain or a burning sensation when urinating, straining or pain when emptying the bladder, laboratory blood tests may show changes in blood fat levels, an increase in the amount of red blood cells (increase in haematocrit), and changes related to kidney function (decrease in filtration rate and increase in blood creatinine), increased urination (if you have heart failure)
- urine tests indicating sugar in urine in heart failure patients.

The following side effects have been reported but the frequency for them to occur is not known:
- phimosis (a tight foreskin that cannot be fully retracted to expose the head of the penis) with symptoms that may include pain, redness, or swelling of the foreskin, discharge from the foreskin, white ring or scar tissue around the opening of the foreskin, pain or burning sensation during urination, bulging of the foreskin during urination.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects
If you get side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website. By reporting side effects, you can help provide more information on the safety of EMPAGLIFLOZIN PD.
You can also send an email directly to the company, pharmacovigilance@pharmadynamics.co.za, to ensure safety of the product.

5. How to store EMPAGLIFLOZIN PD
Store all medicines out of reach of children.
Store at or below 25 °C.
Keep container well closed. Protect from light and moisture.
Do not use after the expiry date stated on the carton. Return all unused medicine to your pharmacist.
Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information
What EMPAGLIFLOZIN PD contains:
The active substance is empagliflozin.
EMPAGLIFLOZIN 10 mg PD: Each film coated tablet contains empagliflozin 10 mg.
EMPAGLIFLOZIN 25 mg PD: Each film coated tablet contains empagliflozin 25 mg.

The other ingredients are:
Tablet cores:
Croscarmellose sodium, colloidal silicon dioxide, hydroxypropyl cellulose, lactose monohydrate, magnesium stearate, microcrystalline cellulose.

Film coating: (Opadry Yellow)
HPMC (hypromellose), iron oxide yellow, macrogol/PEG, titanium dioxide.

What EMPAGLIFLOZIN PD looks like and contents of the pack
EMPAGLIFLOZIN 10 mg PD: Pale yellow, round, debossed with "L75" on one side and on the other side plain, film coated tablets.
EMPAGLIFLOZIN 25 mg PD: Pale yellow, oval, debossed with 'LU' on one side and 'E65' on the other side, film coated tablets.

EMPAGLIFLOZIN PD tablets are available in:
EMPAGLIFLOZIN 10 mg PD:
30, 60 and 90 tablets: 50 mL round opaque white, 33 mm neck HDPE bottles, with a child resistant cap and printed heat-seal liner, containing 30, 60 or 90 tablets, packed in a printed outer carton.
500 tablets: 60 mL round opaque white 33 mm neck HDPE bottles, with a child resistant cap and printed heat-seal liner, containing 500 tablets.
Not all pack sizes are marketed.

EMPAGLIFLOZIN 25 mg PD:
30, 60 and 90 tablets: 50 mL round opaque white, 33 mm neck HDPE bottles, with a child resistant cap and printed heat-seal liner, containing 30, 60 or 90 tablets, packed in a printed outer carton.
500 tablets: 150 mL round opaque white 38 mm neck HDPE bottles, with a child resistant cap and printed heat-seal liner, containing 500 tablets.
Not all pack sizes are marketed.

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EMPAGLIFLOZIN 10 mg PD: A56/21.2/0973
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PASIËNTINLIGTINGSBLAD

SKEDULERINGSTATUS S4

EMPAGLIFLOZIN PD 10 mg filmbedekte tablette
EMPAGLIFLOZIN PD 25 mg filmbedekte tablette
Empagliflosien
EMPAGLIFLOZIN PD bevat suiker (laktosemonohidraat)
45,2 mg per 10 mg tablet en 113 mg per 25 mg tablet.
Wesenlik 'natriumvry'.

Lees hierdie hele inligtingsblad noukeurig deur, voordat u begin om EMPAGLIFLOZIN PD te gebruik
- Hou hierdie inligtingsblad. Dit mag nodig wees vir u om dit weer te lees
- Indien u verdere vrae het, vra asseblief u dokter, apteker, verpleegkundige, of ander gesondheidsorgverskaffer
- EMPAGLIFLOZIN PD is vir u persoonlik voorgeskryf en u moet nie u medisyne met ander mense deel nie. Dit mag skadelik wees vir hulle, selfs al is hulle simptome dieselfde as u eie.

Moet nie EMPAGLIFLOZIN PD gebruik indien u tipe 1 diabetes het nie. EMPAGLIFLOZIN PD word saam met 'n dieet en oefening gebruik om bloedsuikervlakke by volwassenes met tipe 2 diabetes alleenlik, te verlaag. EMPAGLIFLOZIN PD word nie gebruik om liggaamsgewig te beheer nie.

Daar was aanmeldings van metaboliese asidose, insluitend keto-asidose ('n ernstige komplikasie van diabetes), wat ernstig, lewensbedreigend, of noodlottig was, by pasiënte wie EMPAGLIFLOZIN PD neem.

Indien u enige simptome van metaboliese asidose, soos naarheid, braking, maagpyn, uitermatige dors, vinnige en diep asemhaling, verwarring, ongewone slaperigheid of moegheid, 'n soet asemreuk, 'n soet of metaalsmaak in u mond, of 'n vreemde urine- of sweetreuk ervaar, moet u onmiddellik 'n dokter kontak, of u naaste hospitaal besoek (selfs al is u bloedglukosevlak laer as 11mmol/L), sodat u geasseseer kan word vir metaboliese asidose. Verwys ook na "Waarskuwings en voorsorgmaatreëls".

Inhoud van hierdie inligtingsblad

1. Wat EMPAGLIFLOZIN PD is en waarvoor dit gebruik word
EMPAGLIFLOZIN PD bevat die aktiewe bestanddeel empagliflosien.
EMPAGLIFLOZIN PD is lid van 'n groep medisyne wat natrium-glukose ko-transporter 2 (SGLT2) inhibitors genoem word.

EMPAGLIFLOZIN PD werk deur die SGLT2-proteïen in u niere te blokkeer. Dit veroorsaak dat bloedsuiker (glukose), vanuit u urine verwyder word en dus die hoeveelheid suiker in u bloed, verlaag.
Dit is belangrik dat u u dieet en oefeningsplan, soos deur u gesondheidsorgverskaffer aanbeveel word, volhou.

Tipe 2 diabetes mellitus
- EMPAGLIFLOZIN PD word gebruik om tipe 2 diabetes by volwasse pasiënte (ouderdom 18 jaar en ouer), wat nie deur dieet en oefening alleen beheer kan word nie, te behandel.

Wat is tipe 2 diabetes?
Tipe 2 diabetes is 'n siekte wat afkomstig is van beide u gene en u leefstyl. Indien u tipe 2 diabetes het, vervaardig u pankreas nie genoeg insulien, om die glukosevlak in u bloed te beheer nie en u liggaam is nie in staat om sy eie insulien doeltreffend te gebruik nie.
Dit veroorsaak hoë glukosevlakke in u bloed, wat kan lei tot mediese probleme soos hartsiekte, niersiekte, blindheid en swak sirkulasie in u ledemate.

Voorkoming van kardiovaskulêre gevalle
EMPAGLIFLOZIN PD word ook gebruik deur volwassenes met 'tipe 2 diabetes", wie 'n verhoogde kardiovaskulêre risiko toon (gesondheidsprobleme verwant aan u hart en bloedvate), om die risiko vir sterfte weens 'n hartaanval, of ander toestande wat verband hou met u hart of bloedvate, te verlaag, of om die risiko vir hospitalisasie met hartversaking, te verlaag.

Hartversaking
EMPAGLIFLOZIN PD word gebruik om hartversaking by volwassenes met, of sonder tipe 2 diabetes te behandel, om die risiko vir kardiovaskulêre sterfte te verlaag en die moontlikheid van hospitalisasie weens hartversaking, te verminder.
EMPAGLIFLOZIN PD help ook om die verswakking van nierfunksie, te vertraag.

Hartversaking kom voor, wanneer u hart te swak of styf is, om behoorlik te funksioneer. Dit kan lei tot ernstige mediese probleme en die behoefte vir hospitaalsorg. Die mees algemne simptome van hartversaking is asemnood, voel moeg, of is oor die algemeen baie moeg en enkelswelling.

EMPAGLIFLOZIN PD help om u hart te beskerm teen verdere verswakking en verlig u simptome.

Chroniese niersiekte
EMPAGLIFLOZIN PD word gebruik deur volwassenes met chroniese niersiekte, om die risiko vir die volgende te verlaag:
- vordering van niersiekte, of sterfte weens hart- of bloedvatprobleme
- hospitalisasie weens enige oorsaak.

Chroniese niersiekte is 'n langtermyn toestand. Dit mag veroorsaak word deur ander siektes soos diabetes en hoë bloeddruk, of selfs deur u eie immuunstelsel wat die niere aanval. Sou u aan chroniese niersiekte ly, mag u niere geleidelik die vermoë om die bloed behoorlik te suiwer en te filtreer, verloor. Dit mag lei tot ernstige mediese probleme, soos geswelde bene, hartversaking of die behoefte vir hospitaalsorg. EMPAGLIFLOZIN PD help om u nierfunksie te beskerm.

2. Wat u nodig het om te weet, voordat u EMPAGLIFLOZIN PD neem
Moet nie EMPAGLIFLOZIN PD neem:
- indien u allergies is vir emagliflosien, of enige van die ander bestanddele van EMPAGLIFLOZIN PD nie (sien afdeling 6)
- indien u tipe 1 diabetes mellitus het nie ('n chroniese toestand waar die pankreas, min of geen insulien vervaardig nie)
- indien u gediagnoseer is met keto-asidose nie ('n ernstige komplikasie van diabetes, wat voorkom wanneer u liggaam hoë bloedsuurvlakke, wat ketone genoem word, vervaardig)
- indien u swanger is, of u baba borsvoed nie.

Waarskuwings en voorsorgmaatreëls
Neem spesiale sorg met EMPAGLIFLOZIN PD:
- indien u tipe 1 diabetes het (u liggaam vervaardig geen insulien). EMPAGLIFLOZIN PD moet nie gebruik word om tipe 1 diabetes te behandel nie
- indien u vinnige gewigsverlies, naarheid of braking, maagpyn, uitermatige dors, vinnige en diep asemhaling, verwarring, ongewone slaperigheid of moegheid, 'n soet asemreuk, 'n soet- of metaalsmaak in u mond, of 'n vreemde reuk van u urine of sweet ervaar, kontak 'n dokter of u naaste hospitaal onmiddellik. Hierdie simptome mag 'n teken van "keto-asidose" wees – 'n skaars, maar somtyds lewensgevaarlike probleem wat ontstaan wanneer u liggaam hoë bloedsuurvlakke in u urine of bloed vervaardig (soos bepaal deur bloedtoetse), wat ketone genoem word
  Die risiko vir die ontwikkeling van keto-asidose, mag toeneem met langdurige vas, uitermatige alkoholverbruik, dehidrasie, skielike afname in die insuliendosis, of 'n groter behoefte vir insulien weens 'n groot operasie of ernstige siekte
- indien u 'n verhoging in die volumepersentasie van rooibloedselle in die bloed (bepaal as deel van 'n bloedtoets), opmerk
- indien u aan ernstige nierprobleme ly, of nierdialise ondergaan. U mediese praktisyn mag u dosis tot 10 mg een keer daagliks beperk, of 'n ander medisyne aanbeveel (kyk ook afdeling 3, "Hoe om EMPAGLIFLOZIN PD te neem"). U nierfunksie moet geasseseer word, voordat u begin om EMPAGLIFLOZIN PD te neem, ten minste elke 6 maande
- indien u lewerprobleme het
- indien u 'n verhoogde risiko vir lae bloeddruk het, soos by pasiënte met hartsiekte, 'n geskiedenis van lae bloeddruk het, medisyne neem om hoë bloeddruk te behandel, of 75 jaar oud en ouer is, aangesien 'n toename in urinering weens medikasie, die vloeistofbalans in u liggaam mag beïnvloed en u risiko vir dehidrasie, verhoog
- indien u gebraak het, diarree of koors het, of indien u nie die vermoë het om te eet of drink nie. Hierdie toestande kan dehidrasie veroorsaak. U dokter mag vra dat u die gebruik van EMPAGLIFLOZIN PD staak, totdat u herstel het, om die verlies van te veel liggaamsvloeistof te verhoed
- indien u 'n ernstige nierinfeksie of urienweginfeksie met koors, onderlede het. U dokter mag aanraai dat u die gebruik van EMPAGLIFLOZIN PD staak, totdat u herstel het
- indien u gediagnoseer is met hartversaking ('n chroniese toestand, waar die hart bloed swakker pomp as wat dit behoort)
- praat onmiddellik met u mediese praktisyn indien u:
  - indien u 'n kombinasie van simptome ontwikkel, soos pyn, gevoeligheid, rooiheid, of swelling van die geslagsdele, of die gedeelte tussen die geslagsdele en anus, met koors en 'n algemene ongesteldheid, lig u dokter onmiddellik in. Hierdie simptome mag 'n teken van 'n skaars, maar ernstige, of selfs lewensbedreigende infeksie wees, wat nekrotiserende fassiitis van die perineum, of Fournier se gangreen genoem word en die weefsel onder die vel vernietig. Fournier se gangreen moet onmiddellik behandel word
  - simptome ervaar soos 'n brandgevoel by die geslagsdele, rooiheid, pyn en afskeiding, wat 'n teken van genitale infeksie mag wees
- soos met alle diabetiese pasiënte, is dit belangrik om u voete gereeld te ondersoek en enige ander voetsorgadvies van u gesondheidsorgdeskundige, te volg
- u urine sal positief toets vir suiker, terwyl u EMPAGLIFLOZIN PD neem, as gevolg van die manier hoe hierdie medisyne werk
- indien u 75 jaar oud of ouer is, aangesien dit nie aanbeveel word om hierdie medisyne te begin gebruik, na die ouderdom van 75 jaar nie.

Kinders en adolessente
EMPAGLIFLOZIN PD word nie aanbeveel vir kinders en adolessente jonger as 18 jaar nie, aangesien dit nie nagevors is met hierdie pasiënte nie.

Ander medisyne en EMPAGLIFLOZIN PD
Vertel altyd u gesondheidsorgverskaffer, indien u enige ander medisyne neem. (Dit sluit aanvullende of tradisionele medisyne in).
- indien u litium neem ('n gemoedstabiliserende medisyne, wat gebruik word om sekere geestessiektes te behandel). EMPAGLIFLOZIN PD kan die hoeveelheid litium in u bloed verlaag.

EMPAGLIFLOZIN PD saam met kos en drinkgoed
EMPAGLIFLOZIN PD kan saam met, of sonder kos geneem word.

Swangerskap, borsvoeding en fertiliteit
Indien u swanger is, of borsvoed, vermoed dat u swanger is, of 'n baba beplan, raadpleeg u dokter, apteker of ander gesondheidsorgverskaffer vir advies voordat u EMPAGLIFLOZIN PD gebruik.
Moet nie EMPAGLIFLOZIN PD gebruik indien u swanger is nie. Dit is nie bekend of EMPAGLIFLOZIN PD skadelik is vir die ongebore kind nie. Moet nie EMPAGLIFLOZIN PD gebruik indien u borsvoed nie. Dit is nie bekend of EMPAGLIFLOZIN PD in borsmelk uitgeskei word nie.

Bestuur en die hantering van masjiene:
EMPAGLIFLOZIN PD mag die vermoë om te bestuur en masjiene te hanteer, beïnvloed. Indien u simptome van lae bloedsuiker ervaar, soos bewing, sweet, angs, wasige sig, prikkelende lippe, bleekheid, gemoedsveranderinge of verwarring, terwyl EMPAGLIFLOZIN PD geneem word, moet nie bestuur, of masjiene hanteer nie en kontak u gesondheidsorgverskaffer onmiddellik.
Dit is nie altyd moontlik om te voorspel tot watter mate EMPAGLIFLOZIN PD met die daaglikse aktiwiteite van 'n pasiënt inmeng nie. Pasiënte moet verseker dat hulle nie betrokke raak by bogenoemde aktiwiteite, totdat hulle weet tot watter mate EMPAGLIFLOZIN PD hulle aantas nie.

EMPAGLIFLOZIN PD bevat:
Laktose
Indien u dokter u ingelig het dat u 'n onverdraagsaamheid teenoor sommige suikers toon, kontak u dokter, voordat u hierdie medisyne neem.

Natrium
EMPAGLIFLOZIN PD bevat minder as 1 mmol natrium (0,023 g) per dosis en is dus wesenlik 'natriumvry'.

3. Hoe om EMPAGLIFLOZIN PD te neem
Moet nie medisyne wat vir u voorgeskryf is met enige ander persoon deel nie. Gebruik EMPAGLIFLOZIN PD altyd presies soos deur u dokter aanbeveel word. U moet u dokter of apteker raadpleeg indien u onseker is.

Sluk die tablet heel, met water. U kan die tablet saam met, of sonder kos neem.

Tipe 2 Diabetes
Die gewone EMPAGLIFLOZIN PD dosis is een 10 mg tablet een keer daagliks. U dokter sal besluit of dit nodig is om u dosis na 25 mg een keer per dag te verhoog, sou dit nodig wees om te help om u bloedsuiker te beheer. Toets u bloedsuiker soos u gesondheidsorgverskaffer aanbeveel om te doen. Toepaslike oefening en dieet kan u liggaam help om bloedsuiker meer doeltreffend te gebruik.

Hartversaking of chroniese niersiekte
Die gewone EMPAGLIFLOZIN PD dosis is een 10 mg tablet een keer per dag.

Niersiekte:
Praat met u dokter indien u nierprobleme het. U dokter mag u dosis beperk, of besluit om 'n alternatiewe medisyne voor te skryf.

Lewerprobleme:
Praat met u dokter in geval u aan erge lewersiekte ly, aangesien u dokter dit nodig mag ag om u EMPAGLIFLOZIN PD dosis aan te pas.

Bejaardes:
Daar is baie min ondervinding met pasiënte wie 85 jaar en ouer is. Behandeling met EMPAGLIFLOZIN PD moet nie begin word deur pasiënte ouer as 85 jaar nie.

Onthou om alle medisyne te neem, soos aanbeveel deur u dokter, om die beste resultate vir u gesondheid te verkry.
Dieet en oefening kan u liggaam help om bloedsuiker beter te gebruik. Dit is belangrik om die dieet en oefenings-program soos aanbeveel deur u dokter, vol te hou tydens behandeling met hierdie medisyne.

U dokter sal u vertel vir hoe lank u behandeling met EMPAGLIFLOZIN PD sal duur. Moet nie behandeling vroegtydig staak nie want u bloedsuikervlakke mag weer verhoog.

Indien u onder die indruk is dat die werking van EMPAGLIFLOZIN PD té sterk, of té swak is, vertel u dokter of apteker.

Indien u meer EMPAGLIFLOZIN PD neem as wat u moes:
In die geval van oordosering, raadpleeg u dokter of apteker. Indien beide nie beskikbaar is nie, kontak die naaste hospitaal of gifbeheersentrum.

Simptome van oordosering mag die volgende insluit:
- verhoogde risiko en erns van newe-effekte, soos gelys in afdeling 4.

Indien u vergeet om EMPAGLIFLOZIN PD te neem:
Indien u vergeet om EMPAGLIFLOZIN PD te neem, neem dit so gou as wat u onthou, op dieselfde dag.
Indien u nie 'n tablet op dieselfde dag neem nie, neem die normale dosis, die volgende dag. Moet nie 'n dubbeldosis neem, om op te maak vir die vergete, individuele doserings nie.

Indien u die gebruik van EMPAGLIFLOZIN PD staak:
Moet nie ophou om EMPAGLIFLOZIN PD te neem, sonder om eers u dokter te raadpleeg nie. Indien u tipe 2 diabetes mellitus het, mag u bloedsuikervlakke verhoog, indien u die gebruik van EMPAGLIFLOZIN PD staak.
Indien u enige verdere vrae het omtrent die gebruik van hierdie medisyne, vra u dokter, apteker, of verpleegkundige.

4. Moontlike newe-effekte
EMPAGLIFLOZIN PD kan newe-effekte hê.
Nie alle newe-effekte wat vir EMPAGLIFLOZIN PD aangemeld is, word in hierdie inligtingsblad ingesluit nie. Sou u algemene gesondheid versleg, of indien u enige ongunstige effekte ervaar terwyl u EMPAGLIFLOZIN PD gebruik, raadpleeg asseblief u gesondheidsorgverskaffer vir advies.

Indien enige van die volgende gebeur, staak die gebruik van EMPAGLIFLOZIN PD en vertel u dokter onmiddellik, of gaan na die ongevalle-afdeling by u naaste hospitaal:
- swelling van die gesig, lippe, mond, tong, of keel, wat mag lei tot moeisame asemhaling of slukprobleme
- uitslag of gejeuk
- floute.

Hierdie is alles baie ernstige newe-effekte. Indien u dit ondervind, kon u 'n ernstige allergiese reaksie teenoor EMPAGLIFLOZIN PD ervaar het. U mag dringende mediese aandag, of hospitalisasie benodig.

Vertel u dokter onmiddellik, of gaan na die ongevalle-afdeling by u naaste hospitaal, indien u enige van die volgende opmerk:
- diabetiese keto-asidose (simptome sluit die volgende in: vinnige gewigsverlies, naarheid en braking, maagpyn, uitermatige dors, vinnige en diep asemhaling, verwarring, ongewone slaperigheid of moegheid, 'n soet asemreuk, 'n soet of metaalsmaak in u mond, of 'n vreemde urine-, of sweetreuk)
- pyn of gevoeligheid, gejeuk, swelling in die omgwing van die geslagsdele, of aan die agterkant daarvan, koors of 'n gevoel van algemene ongesteldheid. Hierdie mag simptome van 'n ernstige en lewensgevaarlike infeksie wees, wat Fournier se gangreen genoem word
- simptome ervaar van 'n brandgevoel van die geslagsdele, rooiheid, pyn en afskeiding, wat tekens van 'n genitale infeksie mag wees.

Hierdie is alles ernstige newe-effekte. U mag dringende mediese aandag benodig.

Vertel u dokter indien u enige van die volgende opmerk:
Newe-effekte wat dikwels voorkom:
- genitale swaminfeksie, soos sproei, inflammasie van die neus of keel (nasofaringitis), hoes
- sepsis veroorsaak deur urogenitale infeksie (urosepsis), nierinflammasie as gevolg van bakteriële infeksie (piëlonefritis)
- lae bloedsuiker (hipoglisemie), met simptome wat bewing, sweet, 'n baie angstige of verwarde gevoel, vinnige hartklop, uitermatige honger, hoofpyn, insluit
- gewigsverlies, hoë cholesterolvlakke in u bloed
- oormaat suiker in die urine, toename in urinering
- uitslag, gejeuk
- dors
- hardlywigheid.

Minder algemene newe-effekte:
- dehidrasie (met simptome wat ongewone dors, lighoofdigheid of duiseligheid wanneer u opstaan, flouwording, of bewussynsverlies, mag insluit), lae bloeddruk
- urtikarie (rooi, jeukende swelsels), swelling van die gedeelte onder die vel, of mond
- pyn of 'n brandende sensasie wanneer u urineer, stremming of pyn wanneer u die blaas ledig, laboratoriumtoetse mag veranderinge in bloedvetvlakke aantoon, 'n verhoging in die hoeveelheid rooibloedselle (verhoging in hematokrit) en veranderinge wat verband hou
- met nierfunskie (afname in filtrasietempo en verhoging in bloedkreatinien), toename in urinering (indien u hartversaking het)
- urientoetse wat suiker in die urine aandui, by hartversakingpasiënte.

Die volgende newe-effekte is aangemeld, maar die frekwensie van voorkoms, is onbekend:
- fimose ('n stywe voorhuid wat nie volledig teruggetrek kan word om die kop van die penis te ontbloot nie), met simptome wat pyn, rooiheid of swelling van die voorhuid, afskeiding vanuit die voorhuid, wit ring of littekenweefsel rondom die opening van die voorhuid, pyn of brandende sensasie tydens urinering, uitbulting van die voorhuid tydens urinering.

Indien u enige newe-effekte opmerk, wat nie in hierdie inligtingsblad genoem word nie, lig asseblief u dokter of apteker in.

Aanmelding van newe-effekte
Indien u newe-effekte ervaar, praat met u dokter of apteker. Dit sluit enige moontlike newe-effekte in, wat nie in hierdie inligtingsblad gelys word nie. U kan ook newe-effekte by SAHPRA via die Med Safety toepassing (Medsafety X SAHPRA) en eReporting platform (who-umc.org), wat aanlyn op SAHPRA se webtuiste gevind kan word, aanmeld. U kan help om meer inligting aangaande die veiligheid van EMPAGLIFLOZIN PD in te win, deur newe-effekte aan te meld.
U kan ook'n e-pos direk aan die maatskappy stuur: pharmacovigilance@pharmadynamics.co.za, om die veiligheid van die medisyne te verseker.

5. Hoe om EMPAGLIFLOZIN PD te bewaar
Bewaar alle medisyne buite die bereik van kinders.
Bewaar teen of benede 25 °C.
Hou die houer dig geseël. Beskerm teen lig en vog.
Moet nie gebruik na die vervaldatum wat op die kartonhouer aangedui word nie.
Neem alle ongebruikte medisyne na u apteker terug.
Moet nie ongebruikte medisyne in afvoerpype of rioolstelsels (bv. toilette), weggooi nie.

6. Verpakkingsinhoud en ander inligting
Wat EMPAGLIFLOZIN PD bevat:
Die aktiewe bestanddeel is empagliflosien.
EMPAGLIFLOZIN 10 mg PD: Elke filmbedekte tablet bevat empagliflosien 10 mg.
EMPAGLIFLOZIN 25 mg PD: Elke filmbedekte tablet bevat empagliflosien 25 mg.

Die ander bestanddele is:
Tabletkerne:
Hidroksiepropielsellulose, kolloïdale silikondioksied, kruisgekoppelde natriumkarmellose, laktosemonohidraat, magnesiumstearaat, mikrokristallyne sellulose.

Filmbedekking: (Opadry Geel)
Geel ysteroksied, HPMC (hipromellose), makrogol/PEG, titaandioksied.

Hoe EMPAGLIFLOZIN PD lyk en die verpakkingsinhoud
EMPAGLIFLOZIN 10 mg PD: Liggeel, rond, gedebosseleer met "L75" aan een kant en glad aan die teenoorgestelde kant, filmbedekte tablette.
EMPAGLIFLOZIN 25 mg PD: Liggeel, ovaal, gedebosseleer, met 'LU' aan een kant en 'E65' aan die teenoorgestelde kant, filmbedekte tablette.

EMPAGLIFLOZIN PD tablette is beskikbaar in:
EMPAGLIFLOZIN 10 mg PD:
30, 60 en 90 tablette: 50 mL ronde, ondeursigtige, wit 33 mm nek HDPE bottels, met 'n peuterbestande deksel met gedrukte hitte-seël voering. Houer bevat 30, 60 of 90 tablette.
500 tablette: 60 mL ronde, ondeursigtige, wit 33 mm nek HDPE bottels, met 'n peuterbestande deksel met gedrukte hitte-seël voering. Die houer bevat 500 tablette.
Nie alle verpakkingshoeveelhede word bemark nie.

EMPAGLIFLOZIN 25 mg PD:
30, 60 en 90 tablette: 50 mL ronde, ondeursigtige, wit 33 mm nek HDPE bottels, met 'n peuterbestande deksel met gedrukte hitte-seël voering. Die houer bevat 30, 60 of 90 tablette.
500 tablette: 150 mL ronde, ondeursigtige, wit 38 mm nek HDPE bottels, met 'n peuterbestande deksel met gedrukte hitte-seël voering. Die houer bevat 500 tablette.
Nie alle verpakkingshoeveelhede word bemark nie.

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