SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Glysit Met 5/1000 mg film coated Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains

Dapagliflozin ……5mg

Metformin……1000 mg

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film coated Tablet. Orange, capsule shaped film coated tablet with a breakline on one side and plain on other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Type 2 diabetes mellitus: It is indicated in adults for the treatment of insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise.

4.2 Posology and method of administration

The recommended dose is one or two tablets once daily.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Dapagliflozin

Renal impairment

The glycaemic efficacy of Dapagliflozin is dependent on renal function, and efficacy is reduced in patients who have moderate renal impairment and is likely absent in patients with severe renal impairment.

Hepatic impairment

There is limited experience in clinical studies in patients with hepatic impairment.

Use in patients at risk for volume depletion and/or hypotension

Due to its mechanism of action, Dapagliflozin increases diuresis which may lead to the modest decrease in blood pressure observed in clinical studies.

Diabetic ketoacidosis

Sodium-glucose co-transporter 2 (SGLT2) inhibitors should be used with caution in patients with increased risk of DKA.

Metformin

Lactic acidosis

Lactic acidosis, a very rare, but serious metabolic complication, most often occurs at acute worsening of renal function or cardiorespiratory illness or sepsis. Metformin accumulation occurs at acute worsening of renal function and increases the risk of lactic acidosis. In case of dehydration (severe diarrhoea or vomiting, fever or reduced fluid intake), metformin should be temporarily discontinued and contact with a health care professional is recommended. Medicinal products that can acutely impair renal function (such as antihypertensives, diuretics and NSAIDs) should be initiated with caution in metformin-treated patients. Other risk factors for lactic acidosis are excessive alcohol intake, hepatic insufficiency, inadequately controlled diabetes, ketosis, prolonged fasting and any conditions associated with hypoxia, as well as concomitant use of medicinal products that may cause lactic acidosis. Patients and/or care-givers should be informed of the risk of lactic acidosis, characterised by acidotic dyspnoea, abdominal pain, muscle cramps, asthenia and hypothermia followed by coma.

Renal function

GFR should be assessed before treatment initiation and regularly thereafter. Metformin is contraindicated in patients with GFR<30 mL/min and should be temporarily discontinued in the presence of conditions that alter renal function.

Cardiac function

Patients with heart failure are more at risk of hypoxia and renal insufficiency. For patients with acute and unstable heart failure, metformin is contraindicated.

Administration of iodinated contrast agents

Metformin should be discontinued prior to or at the time of the imaging procedure and not restarted until at least 48 hours after, provided that renal function has been re-evaluated and found to be stable.

Surgery

Metformin must be discontinued at the time of surgery under general, spinal or epidural anaesthesia. Therapy may be restarted no earlier than 48 hours following surgery or resumption of oral nutrition, provided renal function is stable.

4.5 Interaction with other medicinal products and other forms of interaction

Dapagliflozin

Diuretics

Dapagliflozin may add to the diuretic effect of thiazide and loop diuretics and may increase the risk of dehydration and hypotension.

Insulin and insulin secretagogues

A lower dose of insulin or an insulin secretagogue may be required to reduce the risk of hypoglycaemia when used in combination with Dapagliflozin.

Metformin

Alcohol

Alcohol intoxication is associated with an increased risk of lactic acidosis, particularly in case of fasting, malnutrition or hepatic impairment.

Iodinated contrast agents

Metformin must be discontinued prior to or at the time of the imaging procedure and not restarted until at least 48 hours after, provided renal function is stable.

Combinations requiring precautions for use

NSAIDs, ACE inhibitors, angiotensin II receptor antagonists and diuretics (especially loop diuretics) can adversely affect renal function which may increase the risk of lactic acidosis. Close monitoring of renal function is necessary.

Organic cation transporters (OCT)

Metformin is a substrate of both transporters OCT1 and OCT2. Inhibitors of OCT1 (verapamil) may reduce efficacy; inducers (rifampicin) may increase absorption/efficacy; inhibitors of OCT2 (cimetidine, dolutegravir, ranolazine, trimethoprim, vandetanib, isavuconazole) may decrease renal elimination and increase metformin plasma concentration; inhibitors of both OCT1 and OCT2 (crizotinib, olaparib) may alter efficacy and renal elimination.

4.6 Fertility, pregnancy and lactation

Dapagliflozin

Pregnancy

There are no data from the use of Dapagliflozin in pregnant women. Studies in rats have shown toxicity to the developing kidney corresponding to the second and third trimesters of human pregnancy. Use is not recommended during the second and third trimesters of pregnancy. Treatment should be discontinued when pregnancy is detected.

Breast-feeding

It is unknown whether Dapagliflozin and/or its metabolites are excreted in human milk. Dapagliflozin should not be used while breast-feeding.

Metformin

Pregnancy

Metformin crosses the placenta. Data on more than 1000 exposed pregnancy outcomes indicate no increased risk of congenital abnormalities or feto/neonatal toxicity. Metformin can be considered during pregnancy if clinically needed, as an addition or alternative to insulin.

Breast-feeding

Metformin is excreted into human breast milk; no adverse effects observed in breastfed infants, but breast-feeding is not recommended due to limited data.

Fertility

Fertility of male or female rats was unaffected by metformin at doses as high as 600 mg/kg/day.

4.7 Effects on ability to drive and use machines

Glysit Met has no or negligible influence on the ability to drive and use machines. Patients should be alerted to the risk of hypoglycaemia.

4.8 Undesirable effects

Dapagliflozin

Common: Vulvovaginitis, balanitis and related genital infections; urinary tract infection. Very common: Hypoglycaemia (when used with SU or insulin). Uncommon: Fungal infection, volume depletion, thirst, constipation, dry mouth. Common: Dizziness, rash, back pain. Very rare: Necrotising fasciitis of the perineum (Fournier's gangrene), angioedema. Rare: Diabetic ketoacidosis.

Metformin

Common: Vitamin B12 decrease/deficiency. Very rare: Lactic acidosis. Common: Taste disturbance. Very common: Gastrointestinal disorders (nausea, vomiting, diarrhoea, abdominal pain, loss of appetite) occurring most frequently during initiation of therapy. Very rare: Isolated reports of liver function test abnormalities/hepatitis; skin reactions such as erythema, pruritus, urticaria.

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

Dapagliflozin

Dapagliflozin did not show any toxicity in healthy subjects at single oral doses up to 500 mg (50 times the maximum recommended human dose), with

detectable glucose in urine for a dose-related period, no reports of dehydration, hypotension or electrolyte imbalance, and no clinically meaningful effect on QTc interval.

Metformin

Hypoglycaemia has not been seen with metformin doses up to 85 g, although lactic acidosis has occurred. Lactic acidosis is a medical emergency treated in hospital; haemodialysis is the most effective method to remove lactate and metformin.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Dapagliflozin

The SGLT2 is the predominant renal transporter responsible for glucose reabsorption. Dapagliflozin improves fasting and post-prandial plasma glucose by reducing renal glucose reabsorption, leading to urinary glucose excretion, independent of insulin secretion and action.

Metformin

Metformin is a biguanide with antihyperglycaemic effects, lowering basal and postprandial plasma glucose without stimulating insulin secretion. It acts by reducing hepatic glucose production, increasing peripheral insulin sensitivity, and delaying intestinal glucose absorption; it also favourably affects lipid metabolism (reduces total cholesterol, LDL cholesterol and triglycerides).

5.2 Pharmacokinetic properties

Dapagliflozin

Absorption: Rapidly absorbed, Cmax at ~2h, absolute oral bioavailability 78% (10 mg dose). Distribution: ~91% protein bound, Vd 118 L. Biotransformation: Extensively metabolised to inactive dapagliflozin 3-O-glucuronide via UGT1A9. Elimination: Terminal half-life 12.9 hours; primarily eliminated via urinary excretion with less than 2% as unchanged drug.

Metformin

Absorption: Cmax at ~2.5h, absolute bioavailability 50-60%. Distribution: Negligible protein binding, Vd 63-276 L. Elimination: Renal clearance >400 mL/min; terminal half-life ~6.5 hours; excreted unchanged in urine.

5.3 Preclinical safety data

Dapagliflozin

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and fertility. Direct/indirect exposure in juvenile/pregnant rats was associated with renal pelvic and tubular dilatations in progeny.

Metformin

Preclinical data reveal no special hazard for humans based on conventional studies on safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and reproductive toxicity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

- Microcrystalline cellulose 101 USP
- Sodium lauryl sulphate BP
- Povidone K 30 BP
- Partially pregelatinized starch 1500 BP
- Sodium starch glycolate BP
- Magnesium stearate BP
- Aerosil BP
- Croscarmellose sodium BP

Film coating:

- Hypromellose BP
- Propylene glycol BP
- Purified Talc BP
- Titanium dioxide BP
- Sunset aluminium lake colour

6.2 Incompatibilities

Not Applicable.

6.3 Shelf life

2 Years.

6.4 Special precautions for storage

Store in a dry place below 30°C. Protect from light. Keep all medicines out of the reach of children.

6.5 Nature and contents of container

Aluminium/Aluminium blister pack; 28 tablets packed in blisters in cartons with literature insert.

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER(S)

H2022/CTD10273/23018

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10. DATE OF REVISION OF THE TEXT

22-08-2026