

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

DAPAGOOD SM 100 TABLET

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Dapagliflozin Propanediol monohydrate

Eq. to Dapagliflozin 10 mg

Sitagliptin phosphate Monohydrate USP

Eq. To Sitagliptin 100mg

Metformin Hydrochloride USP 500 mg

(Extended Release)

Excipients of know effect:

Each Tablet Contains 65 mg of Lactose

For a full list of excipients see section 6.1.

3. PHARMACEUTICAL FORM

Tablet

Yellow & white colour, Caplet shaped bilayer uncoated tablets scored on one side and other side plain.

4. CLINICAL PARTICULARS:

4.1 Therapeutic indications

DAPAGOOD SM 100 is combination of three antidiabetic medicines. Dapagliflozin increases urinary glucose excretion and reduces blood glucose levels. Metformin decreases the amount of glucose you absorb from your food and the amount of glucose made by the liver. Metformin also increases the body's response to insulin, a natural substance that controls the amount of glucose in the blood. Sitagliptin helps control blood sugar levels by increasing substances (incretins) in the body that make the pancreas release more insulin. It also signals the liver to stop producing sugar (glucose) when there is too much sugar in the blood.

4.2 Posology and method of administration

Posology

The recommended dose is one tablet once daily. Each tablet contains a fixed dose of dapagliflozin, metformin, sitagliptin

Method of administration

The tablets should be taken with some water. They may be taken with meals.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients any type of acute metabolic acidosis

(such as lactic acidosis, diabetic ketoacidosis) diabetic pre-coma; severe renal failure (GFR < 30 mL/min) ;

acute conditions with the potential to alter renal function such as:

- dehydration,
- severe infection,
- shock,
- intravascular administration of iodinated contrast agents;
- acute or chronic disease which may cause tissue hypoxia such as:
 - cardiac or respiratory failure,
 - recent myocardial infarction,
 - shock;
 - hepatic impairment;
 - acute alcohol intoxication, alcoholism;
 - breast-feeding.

4.4 Special warnings and precautions for use

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), DAPAGOOD SM 100 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 non-steroidal anti-inflammatory drugs [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

Acute pancreatitis: Use of DPP-4 inhibitors has been associated with a risk of developing acute pancreatitis. Patients should be informed of the characteristic symptom of acute pancreatitis: persistent, severe abdominal pain. Resolution of pancreatitis has been observed after discontinuation of sitagliptin (with or without supportive treatment), but very rare cases of necrotising or haemorrhagic pancreatitis and/or death have been reported. If pancreatitis is suspected, Sitagliptin/Metformin and other potentially suspect medicinal products should be discontinued; if acute pancreatitis is confirmed, Sitagliptin/Metformin should not be restarted. Caution should be exercised in patients with a history of pancreatitis.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant use not recommended

Alcohol: Alcohol intoxication is associated with an increased risk of lactic acidosis, particularly in cases of fasting, malnutrition or hepatic impairment. Iodinated contrast agents: must 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.

Combinations requiring precautions for use: Some medicinal products can adversely affect renal function, which may increase the risk of lactic acidosis, e.g. NSAIDs, including selective cyclo-oxygenase (COX) II inhibitors, ACE inhibitors, angiotensin II receptor

antagonists and diuretics, especially loop diuretics. When starting or using such products in combination with metformin, close monitoring of renal function is necessary.

Insulin and insulin secretagogues: Insulin and insulin secretagogues, such as sulphonylureas, cause hypoglycaemia. Therefore, a lower dose of insulin or an insulin secretagogue may be required to reduce the risk of hypoglycaemia when used in combination with dapagliflozin

4.6 Pregnancy and Lactation:

Pregnancy: There are no adequate data from the use of sitagliptin, dapagliflozin in pregnant women. Studies in animals have shown reproductive toxicity at high doses. limited amount of data suggests the use of metformin in pregnant women is not associated with an increased risk of congenital malformations.

Breast-feeding: It is unknown whether this medicinal product is excreted in human milk. Available

pharmacodynamic/toxicological data in animals have shown excretion of dapagliflozin/metabolites in milk, as well as pharmacologically-mediated effects in nursing offspring. Metformin is excreted in human milk in small amounts. A risk to the newborns/infants cannot be excluded. This medicinal product should not be used while breast-feeding.

Fertility: The effect of this medicinal product on fertility in humans has not been studied. In male and female rats, dapagliflozin showed no effects on fertility at any dose tested. For metformin, studies in animals have not shown reproductive toxicity.

4.7 Effects on ability to drive and use machines

Dapagliflozin & metformin has no or negligible influence on the ability to drive and use machines. Patients should be alerted to the risk of hypoglycaemia when this medicinal product is used in combination with other glucose-lowering medicinal products known to cause hypoglycaemia. Sitagliptin has no or negligible influence on the ability to drive and use machines. However, when driving or using machines, it should be taken into account that dizziness and somnolence have been reported. In addition, patients should be alerted to the risk of hypoglycaemia when Sitagliptin is used in combination with a sulphonylurea or with insulin.

4.8 Undesirable effects

diarrhoea, Nausea, Vomiting, Flatulence, Polyuria, Dyslipidemia, Genital fungal infection, Nasopharyngitis (inflammation of the throat and nasal passages), Urinary tract infection, Headache, Hypoglycemia (low blood glucose level), Conjunctivitis, Cough

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to National Regulatory Agents.

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4.9 Overdose

Metformin: High overdose or concomitant risks of metformin may lead to lactic acidosis. Lactic acidosis is a medical emergency and must be treated in hospital. In the event of an overdose, it is reasonable to employ the usual supportive measures, e.g., remove unabsorbed material from the gastrointestinal tract, employ clinical monitoring (including obtaining an electrocardiogram), and institute supportive therapy if required.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drugs used in diabetes, Combinations of oral blood glucose-lowering drugs,

ATC code: A10BD

Dapagliflozin, Sitagliptin, Metformin combines antihyperglycaemic medicinal products with complementary mechanisms of action to improve glycaemic control in patients with type 2 diabetes: dapagliflozin, a SGLT2 inhibitor, sitagliptin, a dipeptidyl peptidase 4 (DPP-4) inhibitor, and metformin hydrochloride, a member of the biguanide class.

Dapagliflozin: Increases in the amount of glucose excreted in the urine were observed in healthy subjects and in subjects with type 2 diabetes mellitus following the administration of dapagliflozin. Approximately 70 g of glucose was excreted in the urine per day (corresponding to 280 kcal/day) at a dapagliflozin dose of 10 mg/day in subjects with type 2 diabetes mellitus for 12 weeks. Evidence of sustained glucose excretion was seen in subjects with type 2 diabetes mellitus given dapagliflozin 10 mg/day for up to 2 years.

This urinary glucose excretion with dapagliflozin also results in osmotic diuresis and increases in urinary volume in subjects with type 2 diabetes mellitus. Urinary volume increases in subjects with type 2 diabetes mellitus treated with dapagliflozin 10 mg were sustained at 12 weeks and amounted to approximately 375 mL/day. The increase in urinary volume was associated with a small and transient increase in urinary sodium excretion that was not associated with changes in serum sodium concentrations.

Urinary uric acid excretion was also increased transiently (for 3-7 days) and accompanied by a sustained reduction in serum uric acid concentration. At 24 weeks, reductions in serum uric acid concentrations ranged from -48.3 to -18.3 micromoles/L (-0.87 to -0.33 mg/dL).

The pharmacodynamics of 5 mg dapagliflozin twice daily and 10 mg dapagliflozin once daily were compared in healthy subjects. The steady-state inhibition of renal

glucose reabsorption and the amount of urinary glucose excretion over a 24-hour period was the same for both dosing regimens.

Metformin Hydrochloride: Metformin is a biguanide with anti-hyperglycaemic effects, lowering both basal and postprandial plasma glucose. It does not stimulate insulin secretion and therefore does not produce hypoglycaemia.

Metformin may act via three mechanisms:

- by reduction of hepatic glucose production by inhibiting gluconeogenesis and glycogenolysis;
- by modestly increasing insulin sensitivity, improving peripheral glucose uptake and utilisation in muscle;
- by delaying intestinal glucose absorption.

Metformin stimulates intracellular glycogen synthesis by acting on glycogen synthase. Metformin increases the transport capacity of specific types of membrane glucose transporters (GLUT-1 and GLUT-4).

Sitagliptin: Sitagliptin is an orally-active, potent, and highly selective inhibitor of the dipeptidyl peptidase 4 (DPP-4) enzyme for the treatment of type 2 diabetes. The DPP-4 inhibitors are a class of agents that act as incretin enhancers. By inhibiting the DPP-4 enzyme, sitagliptin increases the levels of two known active incretin hormones, glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP). The incretins are part of an endogenous system involved in the physiologic regulation of glucose homeostasis. Sitagliptin is an orally-active, potent, and highly selective inhibitor of the dipeptidyl peptidase 4 (DPP-4) enzyme for the treatment of type 2 diabetes. The DPP-4 inhibitors are a class of agents that act as incretin enhancers. By inhibiting the DPP-4 enzyme, sitagliptin increases the levels of two known active incretin hormones, glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP). The incretins are part of an endogenous system involved in the physiologic regulation of glucose homeostasis. When blood glucose concentrations are normal or elevated, GLP-1 and GIP increase insulin synthesis and release from pancreatic beta cells. GLP-1 also lowers glucagon secretion from pancreatic alpha cells, leading to reduced hepatic glucose production. When blood glucose levels are low, insulin release is not enhanced and glucagon secretion is not suppressed. Sitagliptin is a potent and highly selective inhibitor of the enzyme DPP-4 and does not inhibit the closely-related enzymes DPP-8 or DPP-9 at therapeutic concentrations. Sitagliptin differs in chemical structure and pharmacological action from GLP-1 analogues, insulin, sulphonylureas or meglitinides, biguanides, peroxisome proliferator-activated receptor gamma (PPAR γ) agonists, alpha-glucosidase inhibitors, and amylin analogues.

5.2 Pharmacokinetic properties

DAPAGLIFLOZIN

Absorption: Dapagliflozin was rapidly and well absorbed after oral administration. Maximum dapagliflozin plasma concentrations ($C_{\max}$) were usually attained within 2 hours after administration in the fasted state. Geometric mean steady-state dapagliflozin $C_{\max}$ and AUC_{τ} values following once daily 10 mg doses of dapagliflozin

were 158 ng/mL and 628 ng h/mL, respectively. The absolute oral bioavailability of dapagliflozin following the administration of a 10 mg dose is 78%.

Distribution: Dapagliflozin is approximately 91% protein bound. Protein binding was not altered in various disease states (e.g. renal or hepatic impairment). The mean steady-state volume of distribution of dapagliflozin was 118 litres.

Biotransformation: Dapagliflozin is extensively metabolised, primarily to yield dapagliflozin 3-O-glucuronide, which is an inactive metabolite. Dapagliflozin 3-O-glucuronide or other metabolites do not contribute to the glucose-lowering effects. The formation of dapagliflozin 3-O-glucuronide is mediated by UGT1A9, an enzyme present in the liver and kidney, and CYP-mediated metabolism was a minor clearance pathway in humans.

Elimination: The mean plasma terminal half-life ($t_{1/2}$) for dapagliflozin was 12.9 hours following a single oral dose of dapagliflozin 10 mg to healthy subjects. The mean total systemic clearance of dapagliflozin administered intravenously was 207 mL/min. Dapagliflozin and related metabolites are primarily eliminated via urinary excretion with less than 2% as unchanged dapagliflozin. After administration of a 50 mg [^{14}C]-dapagliflozin dose, 96% was recovered, 75% in urine and 21% in faeces. In faeces, approximately 15% of the dose was excreted as parent drug.

Linearity: Dapagliflozin exposure increased proportional to the increment in dapagliflozin dose over the range of 0.1 to 500 mg and its pharmacokinetics did not change with time upon repeated daily dosing for up to 24 weeks.

METFORMIN HYDROCHLORIDE

Absorption: After an oral dose of metformin, t_{max} is reached in 2.5 h. Absolute bioavailability of a 500 mg or 850 mg metformin tablet is approximately 50-60% in healthy subjects. After an oral dose, the non-absorbed fraction recovered in faeces was 20-30%.

After oral administration, metformin absorption is saturable and incomplete. It is assumed that the pharmacokinetics of metformin absorption is non-linear. At the usual metformin doses and dosing schedules, steady-state plasma concentrations are reached within 24-48 hours and are generally less than 1 $\mu\text{g/mL}$. In controlled clinical trials, maximum metformin plasma levels (C_{max}) did not exceed 5 $\mu\text{g/mL}$, even at maximum doses.

Distribution: Plasma protein binding is negligible. Metformin partitions into erythrocytes. The blood peak is lower than the plasma peak and appears at approximately the same time. The red blood cells most likely represent a secondary compartment of distribution. The mean V_d ranged between 63-276 l.

Biotransformation

Metformin is excreted unchanged in the urine. No metabolites have been identified in humans.

Elimination: Renal clearance of metformin is > 400 mL/min, indicating that metformin is eliminated by glomerular filtration and tubular secretion. Following an oral dose, the apparent terminal elimination half-life is approximately 6.5 hours.

SITAGLIPTIN

Absorption: Following oral administration of a 100-mg dose to healthy subjects, sitagliptin was rapidly absorbed, with peak plasma concentrations (median T_{max})

occurring 1 to 4 hours post-dose, mean plasma AUC of sitagliptin was 8.52 $\mu\text{M}\cdot\text{hr}$, C_{max} was 950 nM. The absolute bioavailability of sitagliptin is approximately 87 %. Since co-administration of a high-fat meal with sitagliptin had no effect on the pharmacokinetics, sitagliptin may be administered with or without food. Plasma AUC of sitagliptin increased in a dose-proportional manner. Dose-proportionality was not established for C_{max} and $C_{24\text{hr}}$ (C_{max} increased in a greater than dose-proportional manner and $C_{24\text{hr}}$ increased in a less than dose-proportional manner).

Distribution: The mean volume of distribution at steady state following a single 100-mg intravenous dose of sitagliptin to healthy subjects is approximately 198 litres. The fraction of sitagliptin reversibly bound to plasma proteins is low (38 %).

Biotransformation: Sitagliptin is primarily eliminated unchanged in urine, and metabolism is a minor pathway. Approximately 79 % of sitagliptin is excreted unchanged in the urine.

Following a [^{14}C] sitagliptin oral dose, approximately 16 % of the radioactivity was excreted as metabolites of sitagliptin. Six metabolites were detected at trace levels and are not expected to contribute to the plasma DPP-4 inhibitory activity of sitagliptin. In vitro studies indicated that the primary enzyme responsible for the limited metabolism of sitagliptin was CYP3A4, with contribution from CYP2C8.

Elimination: Following administration of an oral [^{14}C] sitagliptin dose to healthy subjects, approximately 100 % of the administered radioactivity was eliminated in faeces (13 %) or urine (87 %) within one week of dosing. The apparent terminal $t_{1/2}$ following a 100-mg oral dose of sitagliptin was approximately 12.4 hours. Sitagliptin accumulates only minimally with multiple doses. The renal clearance was approximately 350 mL/min.

5.3 Preclinical safety data

not applicable

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

HPMC

Sodium CMC

PVPK-30

Isopropyl alcohol

Magnesium stearate

MCCP Plain

Lactose monohydrate

Quinoline yellow lake

Low substituted HPC (LH-11)

Crospovidone

Aerosil

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store below 30°C. Protect from light and moisture.

6.5 Nature and contents of container

10 tablets are packed in ALU-ALU blister, such 3 blisters are packed in one carton with insert coded with batch number, manufacturing date and expiry date.

6.6 Special precautions for disposal and other handling:

Not applicable

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURER

MARKETING AUTHORISATION HOLDER:

ZAIN PHARMA LIMITED

Plot No: 209/13741, Colchester Park,
Go-Down No.1, 2, 3, Off Mombasa Road,
Behind Nice And Lovely House,
P.O. Box: 100167-00101, Nairobi, Kenya

8. MARKETING AUTHORIZATION NUMBER

H2026/CTD11593/25281

9. DATE OF FIRST REGISTRATION/RENEWAL OF THE REGISTRATION

18/02/2026

10. DATE OF REVISION OF TEXT

18/02/2026