SUMMARY OF PRODUCT CHARACTERISTICS
DAPAGOOD S 50 (Dapagliflozin 5 mg and Sitagliptin 50 mg Tablets)

1. NAME OF THE MEDICINAL PRODUCT

DAPAGOOD S 50 (Dapagliflozin 5 mg and Sitagliptin 50 mg Tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 5 mg dapagliflozin (as dapagliflozin propanediol monohydrate) and 50 mg sitagliptin (as sitagliptin phosphate monohydrate USP).

Excipients with known effect:

This medicinal product does not contain excipients with known effect at the quantities present.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet.

White coloured, round shaped, film-coated tablet, plain on both sides.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

DAPAGOOD S 50 is indicated as an adjunct to diet and exercise to improve glycaemic control in adults with type 2 diabetes mellitus who are inadequately controlled on metformin monotherapy, when treatment with both dapagliflozin and sitagliptin is appropriate.

4.2 Posology and method of administration

Posology

The dosage of DAPAGOOD S 50 should be individualised on the basis of the patient's current regimen, effectiveness and tolerability, not exceeding the maximum recommended daily dose of 5 mg dapagliflozin and 50 mg sitagliptin. When used in combination with insulin or an insulin secretagogue (e.g. sulfonylurea), a lower dose of the insulin or insulin secretagogue may be required to reduce the risk of hypoglycaemia.

Renal impairment

DAPAGOOD S 50 is contraindicated in patients with an eGFR less than 45 ml/min/1.73 m², severe renal impairment, end-stage renal disease (ESRD) or patients on dialysis. Sitagliptin dose should be reduced to 50 mg daily in patients with moderate renal impairment (eGFR 30–45 ml/min/1.73 m²). This fixed-dose combination (dapagliflozin 5 mg/sitagliptin 50 mg) is therefore not suitable for patients with moderate to severe renal impairment.

Hepatic impairment

No dose adjustment of sitagliptin is required in patients with mild or moderate hepatic impairment. Dapagliflozin exposure is increased in patients with severe hepatic impairment; DAPAGOOD S 50 is not recommended in this population.

Elderly (≥65 years)

No dose adjustment based on age alone is required. However, renal function should be assessed before initiating and volume status should be monitored, particularly in patients ≥75 years.

Paediatric population

Pharmacokinetics in paediatric populations have not been studied. This medicinal product is not intended for use in children and adolescents.

Method of administration

Oral. DAPAGOOD S 50 can be administered with or without food. Positive urine glucose tests should be expected; monitoring glycaemic control with urine glucose tests is not recommended. The 1,5-AG assay is also unreliable in patients taking SGLT2 inhibitors.

4.3 Contraindications

- Hypersensitivity to dapagliflozin, sitagliptin, or to any of the excipients listed in section 6.1.
- Estimated glomerular filtration rate (eGFR) less than 45 ml/min/1.73 m².
- Severe renal impairment, end-stage renal disease (ESRD) or patients on dialysis.

4.4 Special warnings and precautions for use

Volume depletion

Dapagliflozin causes osmotic diuresis, which may lead to volume depletion. Before initiating DAPAGOOD S 50, assess volume status and correct volume depletion. Monitor for signs and symptoms of volume depletion during therapy, particularly in the elderly, patients with renal impairment, patients with low systolic blood pressure, and patients on diuretics.

Diabetic ketoacidosis (DKA)

Rare cases of DKA, including life-threatening and fatal cases, have been reported with SGLT2 inhibitors. The presentation may be atypical with only moderately elevated blood glucose levels. DKA must be considered if patients present with nausea, vomiting, anorexia, abdominal pain, excessive thirst, difficulty breathing, confusion, unusual fatigue or sleepiness. If DKA is suspected, discontinue DAPAGOOD S 50 immediately and treat promptly. Treatment should be interrupted in patients hospitalised for major surgical procedures or acute serious medical illnesses. Do not use in patients with type 1 diabetes.

Urosepsis and pyelonephritis

Post-marketing cases of urosepsis and pyelonephritis, sometimes requiring hospitalisation, have been reported with SGLT2 inhibitors. Evaluate patients for signs and symptoms of urinary tract infections and treat promptly.

Necrotising fasciitis of the perineum (Fournier's Gangrene)

Serious, life-threatening cases have been reported in patients with diabetes, both female and male, taking SGLT2 inhibitors. Assess patients presenting with pain, tenderness, erythema or swelling in the genital or perineal area along with fever or malaise. If suspected, institute prompt treatment including antibiotics and surgical debridement, and discontinue DAPAGOOD S 50 immediately.

Genital mycotic infections

Dapagliflozin increases the risk of genital mycotic infections. Patients with a history of genital mycotic infections are more likely to develop them. Monitor and treat if indicated.

Hypoglycaemia

The risk of hypoglycaemia is increased when DAPAGOOD S 50 is used in combination with an insulin secretagogue (e.g. sulfonylurea) or insulin. Consider a lower dose of the insulin secretagogue or insulin to reduce the risk.

Pancreatitis

Post-marketing reports of acute pancreatitis, including fatal and non-fatal haemorrhagic or necrotising pancreatitis, have been received with both dapagliflozin and sitagliptin. If pancreatitis is suspected, promptly discontinue DAPAGOOD S 50.

Heart failure — DPP-4 inhibitor class effect

An association between DPP-4 inhibitor treatment and an increased risk of heart failure has been observed in cardiovascular outcome trials for other members of the DPP-4 inhibitor class, evaluated in patients with type 2 diabetes and atherosclerotic cardiovascular disease. Consider the risks and benefits of DAPAGOOD S 50 in patients at risk for heart failure. Observe for signs and symptoms of heart failure during therapy.

Renal function assessment

Post-marketing reports of acute renal failure, sometimes requiring dialysis, have been received with dapagliflozin. Assessment of renal function is recommended prior to initiating DAPAGOOD S 50 and periodically thereafter.

Severe and disabling arthralgia

Post-marketing reports of severe and disabling arthralgia have been received with DPP-4 inhibitors. The time to onset varied from one day to years. Consider DPP-4 inhibitors as a possible cause for severe joint pain and discontinue if appropriate.

Bullous pemphigoid

Post-marketing cases of bullous pemphigoid requiring hospitalisation have been reported with DPP-4 inhibitors. If bullous pemphigoid is suspected, discontinue DAPAGOOD S 50 and refer to a dermatologist.

Hypersensitivity reactions

Post-marketing reports of serious hypersensitivity reactions including anaphylaxis, angioedema and exfoliative skin conditions including SJS have been received. If such reactions occur, promptly stop DAPAGOOD S 50, assess for other potential causes and initiate alternative treatment.

Laboratory test interference
Due to the mechanism of action of dapagliflozin, patients will test positive for glucose in their urine. Use alternative methods to monitor glycaemic control. The 1,5-AG assay is unreliable in patients taking SGLT2 inhibitors.

4.5 Interaction with other medicinal products and other forms of interaction

Digoxin:

Co-administration with sitagliptin 10 mg for 10 days resulted in a slight increase in digoxin AUC (11%) and Cmax (18%). Patients receiving digoxin should be monitored appropriately. No dosage adjustment is recommended.

Insulin secretagogues (sulfonylureas) or insulin:

Co-administration may require lower doses of the insulin secretagogue or insulin to reduce the risk of hypoglycaemia.

Urine glucose tests:

Monitoring glycaemic control with urine glucose tests is not recommended; SGLT2 inhibitors increase urinary glucose excretion and will lead to positive urine glucose tests.

1,5-anhydroglucitol (1,5-AG) assay:

Monitoring glycaemic control with 1,5-AG assay is not recommended as measurements are unreliable in patients taking SGLT2 inhibitors.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no adequate and well-controlled studies in pregnant women. Reproduction studies with sitagliptin in rats and rabbits at up to 125 mg/kg did not impair fertility or harm the foetus. Renal pelvic dilatation and reduced pup body weights were observed with dapagliflozin in a pre/postnatal study in rats at doses corresponding to late second and third trimester of human development. No adverse effects were noted at lower doses. DAPAGOOD S 50 should be used during pregnancy only if clearly needed.

Breast-feeding
Both dapagliflozin and sitagliptin are excreted in the milk of lactating rats. It is not known whether these drugs are excreted in human milk. Due to potential adverse reactions in nursing infants, breast-feeding is not recommended during treatment with DAPAGOOD S 50.

Fertility
No clinical studies on the effect of DAPAGOOD S 50 on human fertility have been conducted.

4.7 Effects on ability to drive and use machines

DAPAGOOD S 50 has no or negligible influence on the ability to drive and use machines. Patients should be alerted to the risk of hypoglycaemia when used in combination with a sulfonylurea or insulin.

4.8 Undesirable effects

Summary of the safety profile — Dapagliflozin
The most common adverse reactions (≥5%) with dapagliflozin were female genital mycotic infections, nasopharyngitis and urinary tract infections.

Laboratory findings: Small increases in serum creatinine and decreases in eGFR (haemodynamic, reversible on discontinuation); increases in haematocrit (mean +2.30% vs −0.33% for placebo at week 24); modest increases in LDL cholesterol; decreases in serum bicarbonate in some patients on combination therapy.

Summary of the safety profile — Sitagliptin
Adverse reactions reported in ≥5% of patients treated with sitagliptin and more commonly than placebo: upper respiratory tract infection, nasopharyngitis and headache. Hypoglycaemia occurred more commonly in add-on to sulfonylurea and add-on to insulin studies.

Laboratory findings: Small increase in white blood cell count (approximately 200 cells/µL, not clinically relevant).

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 via the National Regulatory Authority.

4.9 Overdose

Dapagliflozin

There were no reports of overdose during clinical development. Employ supportive measures as dictated by the patient's clinical status. The removal of dapagliflozin by haemodialysis has not been studied.

Sitagliptin

Single doses of up to 800 mg sitagliptin were administered to healthy subjects with a maximum mean QTc increase of 8.0 msec at 800 mg — not considered clinically significant. If overdose occurs, employ usual supportive measures. Sitagliptin is modestly dialyzable; approximately 13.5% of the dose is removed over a 3–4 hour haemodialysis session.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antihyperglycaemic agents. ATC codes: Dapagliflozin: A10BK01; Sitagliptin: A10BH01.

Mechanism of action

DAPAGOOD S 50 combines two antihyperglycaemic agents with complementary mechanisms of action to improve glycaemic control in patients with type 2 diabetes: dapagliflozin, a sodium-glucose cotransporter 2 (SGLT2) inhibitor, and sitagliptin, a dipeptidyl peptidase-4 (DPP-4) inhibitor.

Dapagliflozin: SGLT2, expressed in the proximal renal tubules, is responsible for the majority of filtered glucose reabsorption. By inhibiting SGLT2, dapagliflozin reduces reabsorption of filtered glucose, lowers the renal threshold for glucose, and increases urinary glucose excretion. This mechanism is independent of insulin and contributes to a low risk of hypoglycaemia. Dapagliflozin also reduces sodium reabsorption and increases sodium delivery to the distal tubule, which may influence pre- and afterload of the heart and downregulate sympathetic activity.

Sitagliptin: Sitagliptin is a DPP-4 inhibitor that slows the inactivation of incretin hormones (GLP-1 and GIP). The increased active incretin levels enhance insulin synthesis and release from pancreatic beta cells, and reduce glucagon secretion from alpha cells, in a glucose-dependent manner. Sitagliptin demonstrates high selectivity for DPP-4 and does not inhibit DPP-8 or DPP-9 at therapeutic concentrations.

5.2 Pharmacokinetic properties

Dapagliflozin

Absorption: Cmax reached within 2 hours under fasting conditions. Absolute oral bioavailability 78% following 10 mg dose. A high-fat meal decreases Cmax by up to 50% and prolongs Tmax by approximately 1 hour, but does not alter AUC; can be taken with or without food.

Distribution: Approximately 91% protein bound. Not altered in renal or hepatic impairment.

Metabolism: Primarily mediated by UGT1A9 to dapagliflozin 3-O-glucuronide (inactive; 61% of dose). CYP-mediated metabolism is a minor clearance pathway.

Elimination: Primarily renal. Following a 50 mg dose, 75% of radioactivity excreted in urine and 21% in faeces. Mean plasma terminal half-life approximately 12.9 hours.

Sitagliptin

Absorption: Rapidly absorbed; median Tmax 1–4 hours post-dose. Absolute bioavailability approximately 87%. No effect of high-fat meal on pharmacokinetics.

Distribution: Mean volume of distribution at steady state approximately 198 litres. Low plasma protein binding (38%).

Metabolism: Primarily eliminated unchanged in urine (~79%). Minor metabolism via CYP3A4 (with CYP2C8 contribution). Six metabolites detected at trace levels; not expected to contribute to DPP-4 inhibitory activity.

Elimination: Approximately 100% eliminated in urine (87%) or faeces (13%) within one week. Apparent terminal t½ approximately 12.4 hours. Renal clearance approximately 350 ml/min (involves active tubular secretion via hOAT-3 and P-gp). Sitagliptin is modestly dialyzable (approximately 13.5% removed per session).

Special populations

Renal impairment — Dapagliflozin: At steady-state with 20 mg once daily, systemic exposures were 45%, 2.04-fold and 3.03-fold higher in mild, moderate and severe renal impairment, respectively, compared to

normal renal function. Higher dapagliflozin exposure in renal impairment did not result in correspondingly higher 24-hour urinary glucose excretion. Use is contraindicated when eGFR <45 ml/min/1.73 m².

Renal impairment — Sitagliptin: Approximately 2-fold AUC increase in moderate renal impairment; approximately 4-fold increase in severe renal impairment and ESRD. Dose reduction to 50 mg daily is recommended for moderate renal impairment.

Hepatic impairment — Dapagliflozin: In mild/moderate impairment, Cmax and AUC increased up to 12% and 36%, respectively (not clinically meaningful). In severe hepatic impairment, up to 40% and 67% increases were observed. Not recommended in severe hepatic impairment.

Hepatic impairment — Sitagliptin: Mean AUC and Cmax increased approximately 21% and 13%, respectively, in moderate hepatic impairment. Not clinically meaningful; no dose adjustment required.

5.3 Preclinical safety data

No animal studies have been conducted with the combined dapagliflozin and sitagliptin product to evaluate effects.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

The following excipients are present in the film-coated tablet:

No.	Ingredient
1	Microcrystalline cellulose
2	Dibasic calcium phosphate
3	Purified water
4	Crospovidone
5	Low-substituted hydroxypropylcellulose (LH-11)
6	Magnesium stearate
7	White film coat
8	Polyethylene glycol 400 (PEG 400)
9	Isopropyl alcohol
10	Dichloromethane

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store below 30°C. Protect from light and moisture. Keep out of the reach and sight of children.

6.5 Nature and contents of container

10 tablets packed in one ALU-ALU blister; 3 such blisters packed in one carton with package insert. Pack size: 30 tablets.

6.6 Special precautions for disposal and other handling

No special requirements. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

ZAIN PHARMA LTD.

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 AUTHORISATION NUMBER (PPB REGISTRATION NUMBER)

CTD11589

9. DATE OF FIRST AUTHORISATION / RENEWAL OF AUTHORISATION

13.01.2025

10. DATE OF REVISION OF THE TEXT

03.01.2026