# SUMMARY OF PRODUCT CHARACTERISTICS

**DAPAGOOD M 1000 (Dapagliflozin 10 mg / Metformin Hydrochloride 1,000 mg Extended-Release Tablets)**

## 1. NAME OF THE MEDICINAL PRODUCT

DAPAGOOD M 1000 (Dapagliflozin 10 mg and Metformin Hydrochloride 1,000 mg Extended-Release Tablets)

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each extended-release tablet contains dapagliflozin propanediol monohydrate equivalent to dapagliflozin 10 mg and metformin hydrochloride USP 1,000 mg (extended-release).

**Excipients with known effect:**

Each tablet contains 20 mg lactose monohydrate. For warnings, see section 4.4.

For a full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Extended-release tablet.

(Tablet description to be confirmed from approved CTD dossier.)

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

DAPAGOOD M 1000 is indicated in adults for the treatment of type 2 diabetes mellitus as an adjunct to diet and exercise:

- In patients insufficiently controlled on their maximally tolerated dose of metformin alone.
- In combination with other medicinal products for the treatment of diabetes in patients insufficiently controlled with metformin and those products.
- In patients already being treated with the combination of dapagliflozin and metformin as separate tablets.

### 4.2 Posology and method of administration

**Posology**

The recommended dose of DAPAGOOD M 1000 is one tablet twice daily, taken with meals, to reduce the gastrointestinal adverse reactions associated with metformin. Treatment should be initiated at a dose that provides dapagliflozin 10 mg per day, with the metformin dose based on the patient's current metformin dose or as recommended by the physician. The dose should be titrated gradually to improve gastrointestinal tolerability.

If a dose is missed, it should be taken as soon as remembered. If it is almost time for the next dose, the missed dose should be skipped and dosing resumed at the regular time. Double doses should not be taken on the same day.

**Renal impairment**

Dapagliflozin: DAPAGOOD M 1000 should not be initiated in patients with GFR <60 ml/min. Discontinue if GFR persistently falls below 45 ml/min. The glycaemic efficacy of dapagliflozin is reduced in moderate renal impairment and is likely absent in severe renal impairment.

Metformin: Contraindicated in patients with GFR <30 ml/min. Use with caution and close renal function monitoring in patients with GFR 30–60 ml/min. Renal function must be assessed before initiation and monitored at least 2–4 times annually in patients with GFR <60 ml/min and in elderly patients.

**Hepatic impairment**

DAPAGOOD M 1000 is contraindicated in patients with hepatic impairment. Metformin use is contraindicated in hepatic impairment as it may impair lactate metabolism and increase the risk of lactic acidosis.

**Elderly (≥65 years)**

Elderly patients may be at greater risk for volume depletion and more likely to be treated with diuretics and/or antihypertensives. Renal function should be monitored regularly. A dose lower than the maximum recommended dose should be considered based on renal function and tolerability.

**Paediatric population**
Safety and efficacy in children and adolescents below 18 years of age have not been established. No data are available.

**Method of administration**
Oral. Tablets should be swallowed whole and not crushed, cut or chewed. DAPAGOOD M 1000 should be taken twice daily with meals.

## 4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.
- 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 potential to alter renal function such as: dehydration, severe infection, shock.
- Acute or chronic disease that may cause tissue hypoxia such as: cardiac or respiratory failure, recent myocardial infarction, shock.
- Hepatic impairment.
- Acute alcohol intoxication; alcoholism.

## 4.4 Special warnings and precautions for use

**Lactic acidosis**
Lactic acidosis is a very rare but serious metabolic complication that 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 M 1000 should be temporarily discontinued and medical advice sought.

Medicinal products that can acutely impair renal function (antihypertensives, diuretics, NSAIDs) should be initiated with caution in metformin-treated patients. Other risk factors for lactic acidosis include excessive alcohol intake, hepatic insufficiency, inadequately controlled diabetes, ketosis, prolonged fasting and any condition associated with hypoxia. Lactic acidosis is characterised by acidotic dyspnoea, abdominal pain, muscle cramps, asthenia and hypothermia followed by coma. Diagnostic findings are decreased blood pH (<7.35), increased plasma lactate (>5 mmol/L) and an increased anion gap and lactate/pyruvate ratio. If suspected, patients should stop taking DAPAGOOD M 1000 and seek immediate medical attention.

**Renal function**
The glycaemic efficacy of dapagliflozin is dependent on renal function; efficacy is reduced in moderate renal impairment and absent in severe renal impairment. DAPAGOOD M 1000 should not be initiated in patients with GFR <60 ml/min and should be discontinued if GFR persistently falls below 45 ml/min. Renal function should be assessed before initiation and regularly thereafter. For patients with GFR <60 ml/min and elderly patients, renal function should be assessed at least 2–4 times per year. DAPAGOOD M 1000 must be temporarily discontinued in the presence of conditions that alter renal function. Decreased renal function in elderly patients is frequent and asymptomatic; special caution should be exercised when initiating antihypertensive or diuretic therapy or NSAIDs.

**Volume depletion and hypotension**
Dapagliflozin increases diuresis which may lead to a modest decrease in blood pressure. This may be more pronounced in patients with very high blood glucose concentrations. Caution should be exercised in patients for whom a drop in blood pressure could pose a risk (e.g. patients on antihypertensive therapy with a history of hypotension, or elderly patients). In case of intercurrent conditions that may lead to volume depletion, careful monitoring of volume status is recommended. Temporary interruption of treatment is recommended until the depletion is corrected.

**Diabetic ketoacidosis (DKA)**
Rare cases of DKA — including life-threatening and fatal cases — have been reported in patients taking SGLT2 inhibitors including dapagliflozin. In a number of cases, the presentation was atypical with only moderately increased blood glucose values (below 14 mmol/L). The risk of DKA 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. Patients should be assessed for ketoacidosis immediately if these symptoms occur, regardless of blood glucose level. Blood ketone measurement is preferred to urine. If DKA is suspected or diagnosed, dapagliflozin should be discontinued immediately.

Treatment should be interrupted in patients who are hospitalised for major surgical procedures or acute serious medical illnesses. Before initiating dapagliflozin, factors predisposing to ketoacidosis should be considered,

including: low beta-cell function reserve (type 2 diabetes with low C-peptide or LADA); history of pancreatitis; restricted food intake or severe dehydration; insulin dose reduction; increased insulin requirements due to acute illness, surgery or alcohol abuse. SGLT2 inhibitors should be used with caution in these patients.

DAPAGOOD M 1000 should not be used in patients with type 1 diabetes; DKA was reported with common frequency in type 1 diabetes studies.

**Fournier's gangrene (Necrotising fasciitis of the perineum)**

Post-marketing cases of Fournier's gangrene have been reported with SGLT2 inhibitors. This is a rare but serious and potentially life-threatening event requiring urgent surgical intervention and antibiotic treatment. Patients should be advised to seek medical attention if they experience pain, tenderness, erythema or swelling in the genital or perineal area, with fever or malaise. If Fournier's gangrene is suspected, DAPAGOOD M 1000 should be discontinued and prompt treatment instituted.

**Urinary tract infections**

Urinary glucose excretion may be associated with an increased risk of urinary tract infection (UTI). Temporary interruption of treatment should be considered when treating pyelonephritis or urosepsis.

**Lower limb amputations**

An increase in cases of lower limb amputation (primarily of the toe) has been observed in long-term studies with another SGLT2 inhibitor. Whether this is a class effect is unknown. Routine preventative foot care should be counselled in all diabetic patients taking DAPAGOOD M 1000.

**Surgery and iodinated contrast agents**

DAPAGOOD M 1000 must be discontinued at the time of surgery with general, spinal or epidural anaesthesia, and not restarted until at least 48 hours after surgery or resumption of oral nutrition, provided that renal function has been re-evaluated and found to be stable. Intravascular administration of iodinated contrast agents may lead to contrast-induced nephropathy resulting in metformin accumulation and increased risk of lactic acidosis. DAPAGOOD M 1000 should be discontinued prior to, or at the time of, the imaging procedure and not restarted until at least 48 hours after, provided renal function has been re-evaluated and found stable.

**Urine glucose and 1,5-AG assay**

Patients taking DAPAGOOD M 1000 will test positive for glucose in their urine (this is the mechanism of action and should not be misinterpreted as glycosuria of another cause). Monitoring glycaemic control with the 1,5-anhydroglucitol (1,5-AG) assay is not recommended, as results are unreliable in patients taking SGLT2 inhibitors.

**Lactose content**

This product contains 20 mg lactose monohydrate per tablet. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

**Change in clinical status in previously well-controlled patients**

A patient with type 2 diabetes previously well-controlled on this product who develops laboratory abnormalities or a clinical illness (especially a vague and poorly defined illness) should be evaluated promptly for evidence of ketoacidosis or lactic acidosis. Evaluation should include serum electrolytes and ketones, blood glucose and, if indicated, blood pH, lactate, pyruvate and metformin levels. If acidosis of either form occurs, treatment must be stopped immediately and appropriate corrective measures initiated.

## 4.5 Interaction with other medicinal products and other forms of interaction

**Dapagliflozin — pharmacodynamic interactions**

**Diuretics:**

DAPAGOOD M 1000 may add to the diuretic effect of thiazide and loop diuretics and may increase the risk of dehydration and hypotension.

**Insulin and insulin secretagogues (sulfonylureas):**

These agents cause hypoglycaemia. A lower dose of insulin or an insulin secretagogue may be required to reduce the risk of hypoglycaemia when used in combination with DAPAGOOD M 1000.

**Dapagliflozin — pharmacokinetic interactions**

Dapagliflozin is metabolised primarily via glucuronide conjugation mediated by UGT1A9. It does not inhibit or induce CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, or CYP3A4. Drug interactions via these pathways are not expected.

**Rifampicin (UGT inducer):**

Co-administration caused a 22% decrease in dapagliflozin systemic exposure (AUC) with no clinically meaningful effect on 24-hour urinary glucose excretion. No dose adjustment is recommended.

**Mefenamic acid (UGT1A9 inhibitor):**

Co-administration caused a 55% increase in dapagliflozin systemic exposure, with no clinically meaningful effect on 24-hour urinary glucose excretion. No dose adjustment is recommended.

No clinically significant pharmacokinetic interactions with pioglitazone, sitagliptin, glimepiride, voglibose, hydrochlorothiazide, bumetanide, valsartan or simvastatin have been identified.

**Metformin — interactions**

**Cationic drugs (cimetidine) eliminated by renal tubular secretion (not recommended):**

Cimetidine increased metformin AUC by 50% and Cmax by 81%. Close monitoring of glycaemic control, dose adjustment within the recommended posology and changes in diabetic treatment should be considered when such drugs are co-administered.

**Alcohol:**

Alcohol intoxication is associated with increased risk of lactic acidosis, particularly in fasting, malnutrition or hepatic impairment. Alcohol consumption and alcohol-containing medicinal products should be avoided.

**Iodinated contrast agents:**

See section 4.4.

**Glucocorticoids, beta-2 agonists, diuretics (intrinsic hyperglycaemic activity):**

Blood glucose monitoring should be intensified, especially at the start of concomitant treatment. Dose adjustment of DAPAGOOD M 1000 may be required.

**NSAIDs, ACE inhibitors, ARBs, loop diuretics:**

These drugs may adversely affect renal function, increasing the risk of lactic acidosis. Close monitoring of renal function is necessary when starting or using these drugs with DAPAGOOD M 1000.

**Insulin and insulin secretagogues:**

Lower doses may be required to reduce the risk of hypoglycaemia.

## 4.6 Fertility, pregnancy and lactation

**Pregnancy**

There are no data from the use of DAPAGOOD M 1000 or dapagliflozin in pregnant women. Studies in rats have shown dapagliflozin-related toxicity to the developing kidney during the time period corresponding to the second and third trimesters of human pregnancy. Use of this medicinal product is not recommended during the second and third trimesters of pregnancy. When the patient plans to become pregnant and during pregnancy, it is recommended that diabetes is treated with insulin instead, to maintain blood glucose levels as close to normal as possible.

A limited amount of data from the use of metformin in pregnant women does not indicate an increased risk of congenital malformations. Animal studies with metformin do not indicate harmful effects with respect to pregnancy, embryonic or foetal development, parturition or postnatal development. Nevertheless, insulin remains the preferred treatment for diabetes in pregnancy.

**Breast-feeding**

It is unknown whether dapagliflozin or its metabolites are 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 newborn/infant cannot be excluded. DAPAGOOD M 1000 should not be used while breast-feeding.

**Fertility**

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

## 4.7 Effects on ability to drive and use machines

DAPAGOOD M 1000 has no or negligible influence on the ability to drive and use machines. However, patients should be alerted to the risk of hypoglycaemia when DAPAGOOD M 1000 is used in combination with other glucose-lowering medicinal products known to cause hypoglycaemia (insulin, sulfonylureas).

## 4.8 Undesirable effects

**Summary of the safety profile**

DAPAGOOD M 1000 has been demonstrated to be bioequivalent to co-administered dapagliflozin and metformin. In an analysis of 5 placebo-controlled dapagliflozin add-on to metformin studies (623 subjects treated with dapagliflozin 10 mg as add-on to metformin, 523 treated with placebo plus metformin), no

additional adverse reactions were identified for the combination compared with those reported for the individual components.

For dapagliflozin, the primary safety assessment was conducted in a pre-specified pooled analysis of 13 short-term (up to 24 weeks) placebo-controlled studies with 2,360 subjects treated with dapagliflozin 10 mg. In the dapagliflozin cardiovascular outcomes study, 8,574 patients received dapagliflozin 10 mg for a median exposure of 48 months (30,623 patient-years total).

| System Organ Class | Very common (≥1/10) | Common (≥1/100 to <1/10) | Uncommon / Rare / Not known |
|---|---|---|---|
| Infections | | Vulvovaginitis, balanitis and related genital mycotic infections; UTI | Pyelonephritis, urosepsis (uncommon); Fournier's gangrene (not known) |
| Metabolism and nutrition | | Hypoglycaemia (with insulin/SU); volume depletion/dehydration; increased haematocrit | DKA (rare); lactic acidosis (metformin, very rare); hypovolaemia |
| Gastrointestinal | Nausea, vomiting, diarrhoea, abdominal pain (metformin, especially at initiation) | Constipation, dyspepsia | Metallic taste (metformin) |
| Renal and urinary | | Pollakiuria; dysuria (UTI-related) | Worsening renal function (not known) |
| Skin and subcutaneous | | | Angioedema (rare); serious skin reactions (not known) |
| Musculoskeletal | | Back pain | Lower limb amputation (uncommon — toe, primarily) |
| Vascular | | Hypotension/orthostatic hypotension | |
| Investigations | | Increased serum creatinine/decreased eGFR (early, transient); increased haematocrit; LDL-cholesterol increased; weight decreased | Elevated liver enzymes (metformin, not known) |
| Immune system | | | Hypersensitivity reactions including urticaria, angioedema, anaphylaxis (rare/not known) |

**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**

No toxicity was seen in healthy subjects at single oral doses up to 500 mg (50 times the maximum recommended dose). These subjects had detectable glucosuria for a dose-related period, with no reports of dehydration, hypotension, electrolyte imbalance or clinically meaningful QTc change. In clinical studies at doses up to 100 mg daily for 2 weeks, the incidence of hypoglycaemia was slightly higher than placebo and not dose-related. In the event of overdose, appropriate supportive treatment should be initiated as dictated by the patient's clinical status.

**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. The most effective method to remove metformin and lactate is haemodialysis.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drugs used in diabetes, combinations of oral blood glucose-lowering drugs. ATC code: A10BD15.

DAPAGOOD M 1000 combines two anti-hyperglycaemic agents with different and complementary mechanisms of action.

**Dapagliflozin:**

A highly potent (Ki: 0.55 nM), selective and reversible inhibitor of sodium-glucose co-transporter 2 (SGLT2). SGLT2 is selectively expressed in the kidney and is the predominant transporter responsible for reabsorption of glucose from the glomerular filtrate back into the circulation. Dapagliflozin improves both fasting and post-prandial plasma glucose by reducing renal glucose reabsorption, leading to urinary glucose excretion (glucuretic effect). This effect is observed after the first dose, is continuous over the 24-hour dosing interval and is sustained for the duration of treatment. The amount of glucose removed depends on blood glucose concentration and GFR. Dapagliflozin does not impair normal endogenous glucose production in response to hypoglycaemia and acts independently of insulin secretion and insulin action. Approximately 70 g of glucose was excreted in the urine per day at a dapagliflozin dose of 10 mg/day in subjects with type 2 diabetes.

**Metformin:**

A biguanide with anti-hyperglycaemic effects, lowering both basal and postprandial plasma glucose without stimulating insulin secretion (no intrinsic hypoglycaemic effect). Metformin acts by: (1) reduction of hepatic glucose production by inhibiting gluconeogenesis and glycogenolysis; (2) modestly increasing insulin sensitivity and improving peripheral glucose uptake and utilisation in muscle; (3) delaying intestinal glucose absorption. Metformin also has favourable effects on lipid metabolism at therapeutic doses (reduces total cholesterol, LDL-cholesterol and triglycerides) and is associated with stable body weight or modest weight loss.

## 5.2 Pharmacokinetic properties

DAPAGOOD M 1000 combination tablets are bioequivalent to co-administration of corresponding doses of dapagliflozin and metformin hydrochloride administered as individual tablets.

**Dapagliflozin**

Absorption: Rapidly and well absorbed after oral administration; Cmax usually attained within 2 hours in the fasted state. Geometric mean steady-state Cmax 158 ng/mL and AUCτ 628 ng·h/mL following dapagliflozin 10 mg once daily. Absolute oral bioavailability of a 10 mg dose is 78%. Distribution: Approximately 91% protein-bound; not altered by various disease states. Mean steady-state volume of distribution is 118 litres. Biotransformation: Extensively metabolised, primarily to dapagliflozin 3-O-glucuronide (inactive metabolite) via UGT1A9 in liver and kidney; CYP-mediated metabolism is a minor pathway. Elimination: Mean plasma terminal half-life 12.9 hours after a single 10 mg oral dose. Mean total systemic clearance after IV administration is 207 ml/min. Primarily excreted via urine (75%); approximately 21% in faeces (approximately 15% as unchanged parent drug in faeces). Less than 2% excreted as unchanged dapagliflozin in urine.

**Metformin**

Absorption: Tmax 2.5 hours; absolute bioavailability of immediate-release metformin 500–850 mg approximately 50–60%. Absorption is saturable and incomplete; pharmacokinetics of absorption are non-linear. Steady-state plasma concentrations are reached within 24–48 hours and are generally less than 1 µg/mL; Cmax does not exceed 5 µg/mL at maximum doses. Distribution: Plasma protein binding is negligible; metformin partitions into erythrocytes. Mean Vd ranged between 63–276 L. Biotransformation: Metformin is excreted unchanged in urine; no metabolites have been identified in humans. Elimination: Renal clearance >400 ml/min (glomerular filtration + tubular secretion); apparent terminal elimination half-life approximately 6.5 hours. In renal impairment, plasma and blood half-life is prolonged and renal clearance is decreased proportionally.

## 5.3 Preclinical safety data

**Dapagliflozin:**

No special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and fertility. Dapagliflozin did not induce tumours in mice or rats in two-year carcinogenicity studies. Direct administration to weanling juvenile rats and indirect exposure during late pregnancy (corresponding to human second and third trimesters of renal maturation) and lactation were each associated with increased incidence and/or severity of renal pelvic and tubular dilatations in progeny.

**Metformin:**

No special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, and toxicity to reproduction and development.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

| No. | Excipient | Specification |
|---|---|---|
| 1 | Hydroxypropyl methylcellulose K4M (HPMC K4M) | BP |
| 2 | Hydroxypropyl methylcellulose K100 (HPMC K100) | BP |
| 3 | Sodium carboxymethylcellulose (Sodium CMC) | BP |
| 4 | Povidone K-30 (PVP K-30) | BP |
| 5 | Isopropyl alcohol | BP |
| 6 | Magnesium stearate | BP |
| 7 | Microcrystalline cellulose (MCCP plain) | BP |
| 8 | Lactose monohydrate (excipient with known effect — 20 mg per tablet) | BP |
| 9 | Quinoline yellow lake (E104) | IH |
| 10 | Microcrystalline cellulose pH102 (MCCP pH102) | BP |
| 11 | Low-substituted hydroxypropylcellulose (LH-11) | BP |
| 12 | Crospovidone | BP |
| 13 | Colloidal silicon dioxide (Aerosil-200) | BP |
| 14 | Hydroxypropyl methylcellulose E5 (HPMC E5) | BP |
| 15 | Methylene chloride (dichloromethane) | BP |

### 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. 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
Any unused 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)

H2026/CTD11595/25252

## 9. DATE OF FIRST AUTHORISATION / RENEWAL OF AUTHORISATION

16.02.2026

## 10. DATE OF REVISION OF THE TEXT

16.02.2026