

**Brand: Daposit-M™**

**Generic Name: Dapagliflozin 10 mg + Sitagliptin 100 mg + Metformin (Extended Release)**

**500 mg (Fixed-dose combination)**

**Dosage Form: Oral Tablet**

**Composition of Daposit-M™:**

- **Dapagliflozin: 10 mg (Sodium-glucose cotransporter 2 [SGLT2] inhibitor).**
- **Sitagliptin: 100 mg (Dipeptidyl peptidase-4 [DPP-4] inhibitor).**
- **Metformin Hydrochloride (Extended Release): 500 mg (Biguanide).**

**Mechanism of Action:**

**1. Dapagliflozin (SGLT2 Inhibitor):**

- **MOA: Dapagliflozin is a selective Sodium-Glucose Co-Transporter-2 (SGLT2) inhibitor. It works by inhibiting the SGLT2 protein in the kidneys, which is responsible for reabsorbing glucose from the urine back into the bloodstream. By inhibiting this transporter, dapagliflozin increases the excretion of glucose in urine, thereby lowering blood glucose levels.**
- **Effect: Reduces blood glucose levels primarily through the urinary excretion of glucose. It also helps with weight loss and may have beneficial effects on heart failure and kidney function.**

**2. Sitagliptin (DPP-4 Inhibitor):**

- **MOA: Sitagliptin is a Dipeptidyl Peptidase-4 (DPP-4) inhibitor. DPP-4 is an enzyme that deactivates incretin hormones (GLP-1 and GIP), which play a key role in regulating insulin and glucagon secretion. By inhibiting DPP-4, sitagliptin increases the levels of active incretin hormones, which enhances insulin secretion in response to meals and inhibits glucagon release, thus reducing hepatic glucose production.**
- **Effect: Enhances insulin secretion and suppresses glucagon secretion, particularly after meals, helping to lower blood glucose levels.**

**3. Voglibose (Alpha-Glucosidase Inhibitor):**

- **MOA: Voglibose is an alpha-glucosidase inhibitor. It works by inhibiting the activity of enzymes in the small intestine (such as alpha-glucosidase) that break down complex carbohydrates into glucose. By delaying carbohydrate digestion and absorption, voglibose slows the rise in blood glucose levels after meals.**
- **Effect: Reduces postprandial blood glucose spikes by inhibiting carbohydrate breakdown in the gut, thus preventing rapid increases in blood glucose.**

### **Combined Mechanism:**

- **Dapagliflozin:** Lowers blood glucose by increasing glucose excretion in urine.
- **Sitagliptin:** Enhances insulin secretion and inhibits glucagon release.
- **Voglibose:** Slows carbohydrate absorption, preventing postprandial glucose spikes.

Together, these medications Daposit-M™ provide a multi-pronged approach to controlling blood glucose levels:

- **Dapagliflozin** helps with basal glucose control and weight reduction.
- **Sitagliptin** improves insulin response to meals and controls hepatic glucose production.
- **Voglibose** controls postprandial blood sugar increases, complementing the other drugs.

This combination is beneficial in controlling both fasting and postprandial blood glucose levels in individuals with type 2 diabetes.

### **Indications: Daposit-M™**

- **Dapagliflozin 10 mg + Sitagliptin 100 mg + Metformin (ER) 500 mg** is indicated for the treatment of type 2 diabetes mellitus:
  - As an adjunct to diet and exercise to improve glycemic control.
  - In patients who are inadequately controlled on Metformin alone, Sitagliptin alone, or Dapagliflozin alone.
  - It can be used in combination with other antidiabetic agents, including insulin or sulfonylureas, as necessary.

### **Dosage and Administration: Daposit-M™**

- **Starting dose:** Typically, one tablet of Dapagliflozin 10 mg + Sitagliptin 100 mg + Metformin (ER) 500 mg once daily, taken with food, to minimize gastrointestinal side effects, especially from Metformin.
- **Dose titration:** The dose may be increased gradually, based on blood glucose levels. The maximum recommended dose is Dapagliflozin 10 mg + Sitagliptin 100 mg + Metformin (ER) 1000 mg once daily.
- **Administration:** Take the tablet once daily with the evening meal.
- **Renal function:** Kidney function should be evaluated before starting the treatment. Dapagliflozin is contraindicated in patients with severe renal impairment (e.g., eGFR < 30 mL/min/1.73 m<sup>2</sup>).

### **Contraindications: Daposit-M™**

- Hypersensitivity to Dapagliflozin, Sitagliptin, Metformin, or any other components of the combination tablet.
- Severe renal impairment (e.g., eGFR < 30 mL/min/1.73 m<sup>2</sup>).
- Acute or chronic metabolic acidosis, including diabetic ketoacidosis.

- Lactic acidosis (due to Metformin).
- Pregnancy and breastfeeding (Metformin is contraindicated in these conditions, and there is insufficient safety data for Dapagliflozin and Sitagliptin during pregnancy).
- Severe hepatic impairment.
- Hypersensitivity reactions, including angioedema or anaphylaxis, related to Sitagliptin.

#### Warnings and Precautions:

- **Lactic acidosis:** Metformin has been associated with a rare but serious condition called lactic acidosis. Risk factors include renal impairment, dehydration, alcohol abuse, and liver disease. Immediate discontinuation is required if lactic acidosis is suspected.
- **Hypoglycemia:** Sitagliptin and Metformin alone are not typically associated with hypoglycemia, but the combination with other antidiabetic agents (like insulin or sulfonylureas) can increase the risk of hypoglycemia. Monitor blood glucose levels regularly.
- **Renal function:** Regular monitoring of renal function is essential. Dapagliflozin should be discontinued in patients who experience a significant decline in renal function (e.g., eGFR < 45 mL/min/1.73 m<sup>2</sup>).
- **Genital infections:** Dapagliflozin may increase the risk of genital fungal infections. Patients should be advised to report symptoms such as genital pain, itching, or discomfort.
- **Ketoacidosis:** SGLT2 inhibitors, including Dapagliflozin, have been associated with an increased risk of diabetic ketoacidosis (DKA), even in patients without markedly elevated blood glucose levels.
- **Pancreatitis:** There is a potential risk of pancreatitis with Sitagliptin. Patients should be monitored for symptoms such as abdominal pain, nausea, and vomiting.
- **Volume depletion:** Dapagliflozin can lead to volume depletion (dehydration), particularly in patients who are elderly, have renal impairment, or are on diuretics. Proper hydration should be maintained.

#### Drug Interactions:

- **Dapagliflozin:**
  - Can interact with diuretics, RAAS inhibitors (ACE inhibitors, angiotensin receptor blockers), and other antihypertensive agents, which may increase the risk of hypotension and dehydration.
  - Increased risk of acute kidney injury when used with other nephrotoxic drugs.
- **Sitagliptin:**
  - Caution when co-administered with other antidiabetic drugs (such as insulin or sulfonylureas), as this may increase the risk of hypoglycemia.

- CYP450 interactions are minimal with Sitagliptin.
- **Metformin:**
  - Interacts with iodinated contrast agents; discontinue Metformin temporarily before and after procedures requiring contrast agents if renal function is compromised.
  - Corticosteroids, diuretics, and other medications may alter glucose control or renal function.

#### **Side Effects:**

##### **Common side effects:**

- **Dapagliflozin:** Genital fungal infections, urinary tract infections, increased urination, dehydration, hypotension.
- **Sitagliptin:** Headache, nasopharyngitis, upper respiratory tract infection, joint pain, gastrointestinal disturbances.
- **Metformin (ER):** Nausea, diarrhoea, abdominal discomfort, loss of appetite, and a metallic taste.

##### **Serious side effects:**

- Lactic acidosis (due to Metformin).
- Pancreatitis (due to Sitagliptin).
- Hypotension, dehydration, and kidney injury (due to Dapagliflozin).
- Genital infections (due to Dapagliflozin).

##### **Use in Specific Populations:**

- **Pregnancy:** Not recommended during pregnancy. Insulin is generally preferred during pregnancy for blood sugar control.
- **Breastfeeding:** Not recommended, as it is unknown whether Dapagliflozin, Sitagliptin, or Metformin are excreted in breast milk.
- **Pediatrics:** Safety and effectiveness in children have not been established.
- **Geriatrics:** Elderly patients may be more susceptible to side effects such as dehydration or hypotension. Close monitoring is required, particularly for renal function.
- **Renal impairment:** Dapagliflozin is contraindicated in patients with severe renal impairment. For patients with moderate renal impairment, use with caution, and monitor renal function regularly.
- **Hepatic impairment:** Caution is advised for patients with hepatic impairment. Discontinue Metformin in cases of severe liver dysfunction.

##### **Overdose:**

- **Dapagliflozin:** Overdose may result in hypotension, dehydration, and renal impairment. Treatment is symptomatic and supportive.

- **Sitagliptin:** Overdose may cause mild gastrointestinal symptoms. There is no specific antidote, and treatment is generally supportive.
- **Metformin:** Overdose can lead to lactic acidosis, which requires immediate medical intervention. Hemodialysis may be necessary to remove Metformin from the bloodstream.

**Storage:**

- Store at room temperature (15°C to 30°C / 59°F to 86°F).
- Keep in its original container, tightly closed, and away from light and moisture.
- Keep out of reach of children.

**Packaging:**

- Each Alu-Alu strip Daposit-M™ contains 10 tablets.
- Each box of Daposit-M™ contains 10 strips.

**Note:** This summary provides general prescribing information.