GLUCRETA M

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory Only

Abbreviated Prescribing information for GLUCRETA M [Dapagliflozin and Metformin Hydrochloride Extended-Release Tablets]

[Please refer the complete prescribing information available at www.torrentpharma.com]

PHARMACOLOGICAL PROPERTIES:

MECHANISM OF ACTION: *Dapagliflozin*: Sodium-glucose cotransporter 2 (SGLT2), expressed in the proximal renal tubules, is responsible for the majority of the reabsorption of filtered glucose from the tubular lumen. Dapagliflozin is an inhibitor of SGLT2. By inhibiting SGLT2, dapagliflozin reduces reabsorption of filtered glucose and lowers the renal threshold for glucose, and thereby increases urinary glucose excretion. *Metformin hydrochloride*: Metformin improves glucose tolerance in patients with type 2 diabetes, lowering both basal and postprandial plasma glucose. Metformin decreases hepatic glucose production, decreases intestinal absorption of glucose, and improves insulin sensitivity by increasing peripheral glucose uptake and utilization. Metformin does not produce hypoglycemia in either patient with type 2 diabetes or in healthy subjects, except in unusual circumstances, and does not cause hyperinsulinemia.

INDICATIONS: It is indicated as an adjunct to diet and exercise to improve glycaemic control in adults with type 2 diabetes mellitus when treatment with both Dapagliflozin and Metformin is appropriate.

DOSAGE AND ADMINISTRATION: Healthcare providers should individualize the starting dose of Medicine based on the patient's current treatment. Medicine should be taken once daily in the morning with food with gradual dose escalation to reduce the gastrointestinal (GI) side effects due to metformin. Medicine must be swallowed whole and never crushed, cut, or chewed. Dosing may be adjusted based on effectiveness and tolerability while not exceeding the maximum recommended daily dose of 10 mg dapagliflozin and 2000 mg metformin HCl. Tablets should be swallowed whole & not chewed or crushed.

CONTRAINDICATION: Severe renal impairment (eGFR below 30 mL/min/1.73 m^2) or end-stage renal disease, history of a serious hypersensitivity reaction to dapagliflozin or hypersensitivity to metformin hydrochloride. Acute or chronic metabolic acidosis, including diabetic ketoacidosis, with or without coma. Diabetic ketoacidosis should be treated with insulin.

WARNINGS & PRECAUTIONS: *Lactic Acidosis*: Lactic acidosis is a rare, but serious, metabolic complication that can occur due to metformin accumulation during treatment with dapagliflozin and metformin hydrochloride extended-release tablets; when it occurs, it is fatal in approximately 50% of cases. Patients should be cautioned against excessive alcohol intake when taking metformin since alcohol potentiates the effects of metformin hydrochloride on lactate metabolism. In addition, metformin should be temporarily discontinued prior to any intravascular radiocontrast study and for any surgical procedure. *Ketoacidosis*: Reports of ketoacidosis, a serious life-threatening condition requiring urgent hospitalization have been identified in patients with type 1 and type 2 diabetes mellitus receiving sodium-glucose cotransporter 2 (SGLT2) inhibitors, including dapagliflozin. Consider monitoring for ketoacidosis and temporarily discontinuing dapagliflozin and metformin hydrochloride extended-release tablets in other clinical situations known to predispose to ketoacidosis. *Acute Kidney Injury*: Dapagliflozin causes intravascular volume contraction and can cause acute kidney injury. *Urosepsis and Pyelonephritis*: Treatment with SGLT2 inhibitors increases the risk for urinary tract infections. Evaluate patients for signs and symptoms of urinary tract infections and treat promptly, if indicated. *Use in Patients with Renal Impairment*: Metformin is known to be substantially excreted by the kidney and the risk of metformin accumulation and lactic acidosis increases with the degree of impairment of renal function. *Hypotension*: Dapagliflozin causes intravascular volume contraction. *Impaired Hepatic Function*: Therefore, dapagliflozin and metformin hydrochloride extended release tablets should generally be avoided in patients with hepatic impairment. *Alcohol Intake*: Alcohol potentiates the effect of metformin on lactate metabolism.

DRUG INTERACTIONS: *Carbonic Anhydrase Inhibitors*: Consider more frequent monitoring of these patients. *Drugs that Reduce Metformin Clearance*: Consider the benefits and risks of concomitant use. *Alcohol*: Warn patients against excessive alcohol intake while receiving Dapagliflozin and Metformin hydrochloride extended-release tablets. *Insulin or Insulin Secretagogues*: Concomitant use may require lower doses of insulin or the insulin secretagogue to reduce the risk of hypoglycemia. *Drugs Affecting Glycemic Control*: When such drugs are

administered to a patient receiving Dapagliflozin and Metformin hydrochloride extended-release tablets, observe the patient closely for loss of blood glucose control. *Lithium*: Monitor serum lithium concentration more frequently during Dapagliflozin and Metformin hydrochloride extended-release tablets initiation and dosage changes. *Positive Urine Glucose Test*: Monitoring glycemic control with urine glucose tests is not recommended in patients taking SGLT2 inhibitors. *Interference with 1,5-anhydroglucitol (1,5-AG) Assay*: Monitoring glycemic control with 1,5-AG assay is not recommended. Use alternative methods to monitor glycemic control.

ADVERSE REACTIONS: Lactic acidosis, diabetic ketoacidosis in patients with type 1 diabetes mellitus and other ketoacidosis, volume depletion, urosepsis and pyelonephritis, necrotizing fasciitis of the perineum (Fournier's gangrene), use with medications known to cause hypoglycemia, vitamin B12 concentrations, genital mycotic infections, female genital mycotic infections, male genital mycotic infections, nasopharyngitis, urinary tract infections, diarrhea, headache, influenza, nausea, back pain, dizziness, cough, constipation, dyslipidemia, pharyngitis, increased urination, discomfort with urination, pain in extremity.

MARKETED BY:

Torrent Pharmaceuticals Limited.

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(Additional information is available on request)