

ENCELIN DM/ TORGLIP DM

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

Abbreviated Prescribing information for ENCELIN DM/ TORGLIP DM

(Vildagliptin (As sustained release), Dapagliflozin and Metformin Hydrochloride (As sustained release) Tablets (100 mg+10 mg+ 500 mg) and (100 mg+10 mg+ 1000 mg))

[Please refer the complete prescribing information for details].

PHARMACOLOGICAL PROPERTIES:

Mechanism of Action: Dapagliflozin: Dapagliflozin is a reversible inhibitor of sodium-glucose co-transporter 2 (SGLT2) that improves glycaemic control in patients with type 2 diabetes mellitus by reducing renal glucose reabsorption leading to urinary excretion of excess glucose (glucuresis). SGLT2 is selectively expressed in the kidney. SGLT2 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 levels by reducing renal glucose reabsorption leading to urinary excretion of excess glucose. The amount of glucose removed by the kidney through this mechanism is dependent upon the blood glucose concentration and GFR. Dapagliflozin does not impair normal endogenous glucose production in response to hypoglycaemia. Dapagliflozin acts independently of insulin secretion and insulin action. Urinary glucose excretion (glucuresis) induced by Dapagliflozin is associated with caloric loss and reduction in weight. Inhibition of glucose and sodium co-transport by Dapagliflozin is also associated with mild diuresis and transient natriuresis. **Vildagliptin:** The effect of vildagliptin layer results in a rapid and complete inhibition of DPP-4 activity, resulting in increased fasting and postprandial endogenous levels of the incretin hormones GLP-1 (glucagon-like peptide 1) and GIP (glucose-dependent insulinotropic polypeptide). **Metformin HCL:** 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 patients with type 2 diabetes or in healthy subjects, except in unusual circumstances and does not cause hyperinsulinemia. With metformin therapy, insulin secretion remains unchanged while fasting insulin levels and day-long plasma insulin response may actually decrease.

INDICATIONS: It is indicated for the treatment of patients with type 2 diabetes mellitus.

DOSAGE AND ADMINISTRATION: As directed by the Physician. Tablets should be taken orally.

CONTRAINDICATION: Dapagliflozin: History of a serious hypersensitivity reaction to Dapagliflozin, such as anaphylactic reactions or angioedema. Patients who are being treated for glycemic control without established CVD or multiple CV risk factors with severe renal impairment. Patients on dialysis. **Vildagliptin:** Contraindicated in patients with type 1 diabetes, diabetic ketoacidosis. **Metformin:** Metformin are contraindicated in patients with: Severe renal impairment (eGFR below 30 mL/min/1.73 m²). Known 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: Dapagliflozin: *Volume depletion:* Before initiating, assess volume status and renal function in the elderly, patients with renal impairment or low systolic blood pressure, and in patients on diuretics. Monitor for signs and symptoms during therapy. *Urosepsis and Pyelonephritis:* Evaluate for signs and symptoms of urinary tract infections and treat promptly, if indicated. *Hypoglycemia:* Consider a lower dose of insulin or the insulin secretagogue to reduce the risk of hypoglycemia when used in combination with drug. **Vildagliptin:** *Renal impairment:* There is limited experience in patients with ESRD on haemodialysis. Therefore, Vildagliptin should be used with caution in these patients. *Hepatic impairment:* Vildagliptin should not be used in patients with hepatic

impairment, including patients with pre-treatment ALT or AST > 3x ULN. **Artralgia:** Post marketing report shown DPP-4 inhibitors like viladgliptin induced Arthralgia

DRUG INTERACTIONS: No interaction studies have been performed for Dapagliflozin and Vildagliptin SR and Metformin SR tablets. Information available on the individual active substances is as following. **Vildagliptin:** There may be an increased risk of angioedema in patients concomitantly taking ACE-inhibitors. As with other oral antidiabetic medicinal products the hypoglycaemic effect of vildagliptin may be reduced by certain active substances, including thiazides, corticosteroids, thyroid products and sympathomimetic. **Dapagliflozin:** Concomitant use of anhydrase inhibitors (e.g., zonisamide, acetazolamide or dichlorphenamide) with Dapagliflozin and Metformin Hydrochloride Extended release Tablet may increase the risk for lactic acidosis. **Metformin:** Drugs like thiazides and other diuretics, corticosteroids, phenothiazines, thyroid products, estrogens, oral contraceptives, phenytoin, nicotinic acid, sympathomimetics, calcium channel blocking drugs, and isoniazid tend to produce hyperglycemia and may lead to loss of glycemic control.

ADVERSE REACTIONS: Vulvovaginitis, balanitis and related genital infections, Urinary tract infection, Necrotising fasciitis of the perineum (Fournier's gangrene), Fungal infection, Hypoglycaemia (when used with SU or insulin), Volume depletion, Diabetic ketoacidosis (when used in type 2 diabetes mellitus), Dizziness, Constipation, Dry mouth, Rash, Angioedema, Back pain, Dysuria Polyuria, Nocturia, Vulvovaginal pruritus, Pruritus genital, Haematocrit increased^a Creatinine renal clearance decreased during initial treatment^b Dyslipidaemia, Blood creatinine increased during initial treatment, Blood urea increased, Weight decreased

MARKETED BY:



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(Additional information is available on request)