ENCELIN M OD/TORGLIP M OD

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

abbreviated prescribing information for ENCELIN M OD/TORGLIP M OD (Vildagliptin & Metformin Hydrochloride (SR) Tablets) [Please refer the complete prescribing information available at www.torrentpharma.com]

PHARMACOLOGICAL PROPERTIES: The administration of vildagliptin 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 hydrochloride decreases hepatic glucose production, decreases intestinal absorption of glucose and improves insulin sensitivity by increasing peripheral glucose uptake and utilization. Metformin hydrochloride stimulates intracellular glycogen synthesis by acting on glycogen synthase and increase the transport capacity of specific types of membrane glucose transporters (GLUT-1 and GLUT-4)

INDICATION: It is used for the treatment of type-II diabetes mellitus inadequately controlled on metformin monotherapy. Treatment of deep vein thrombosis (DVT) and pulmonary Embolism (PE), and prevention of Recurrent DVT and PE in adult patients.

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

CONTRAINDICATION: 1) Hypersensitivity to vildagliptin or metformin hydrochloride or to any of the excipient. 2) Metabolic acidosis, including lactic acidosis or diabetic ketoacidosis, with or without coma. 3) Radiologic studies involving intravascular administration of iodinated contrast materials, because use of such products may result in acute alteration of renal function.

WARNINGS & PRECAUTIONS: *General:* Vildagliptin is not a substitute for insulin in insulin-requiring patients. Vildagliptin should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. *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. *Liver enzyme monitoring:* Rare cases of hepatic dysfunction (including hepatitis) have been reported. Liver function tests should be performed prior to the initiation of treatment with vildagliptin. Patients who develop increased transaminase levels should be monitored with a second liver function evaluation to confirm the finding. Should an increase in AST or ALT of 3x ULN or greater persist, withdrawal of vildagliptin therapy is recommended. Patients who develop jaundice or other signs suggestive of liver dysfunction should discontinue Vildagliptin. *Pancreatitis:* If pancreatitis is suspected, vildagliptin and other potentially suspect medicinal products should be discontinued. *Lactic Acidosis:* Lactic acidosis is a very rare but serious metabolic complication that most often occurs with acute worsening of renal function, or cardiorespiratory illness or sepsis. In case of dehydration (e.g. due to severe diarrhea or vomiting, fever or reduced fluid intake), the patient should stop taking metformin-containing products and seek immediate medical attention. Medicinal products that can acutely impair renal function (such as antihypertensives, diuretics and NSAIDs) should be initiated with caution in patients treated with metformin-containing products. *Hypoxic states*: Cardiovascular collapse (shock), acute congestive heart failure, acute myocardial infarction and other conditions characterized by hypoxaemia have been associated with lactic acidosis and may also cause prerenal azotmeia. If such events occur in patients receiving metformin-containing products, the medication should be promptly discontinued.

DRUG INTERACTIONS: Vildagliptin: Vildagliptin has low potential for drug interactions. Since vildagliptin is not a cytochrome P (CYP) 450 enzyme substrate nor does it inhibit or induce CYP 450 enzymes, it is not likely to interact with co-medications that are substrates, inhibitors or inducers of these enzymes. Furthermore, vildagliptin does not affect metabolic clearance of co-medicationsmetabolized by CYP 1A2, CYP 2C8, CYP 2C9, CYP 2C19, CYP 2D6, CYP 2E1, and CYP 3A4/5. **Metformin Hydrochloride:** *Furosemide***:** Furosemide increased Cmax and blood AUC of metformin with no change in renal clearance of metformin. Metformin decreased Cmax, blood AUC of furosemide, with no change in renal clearance of furosemide. *Nifedipine:* Nifedipine increased absorption, Cmax and AUC of metformin, and increased excretion of metformin in urine. Metformin had minimal effects on nifedipine. *Glyburide:* Glyburide produced no changes in metformin PK/PD parameters. Decreases in Cmax, blood AUC of glyburide were observed, but were highly variable. Therefore, the clinical significance of this finding was unclear. *Iodinated contrast agents:* Metformin-containing products (such as Galvus Met) must be discontinued prior to or at the time of the imaging procedure and not restarted until at least 48 hours after, provided that renal function has been re-evaluated and found to be stable. *Drugs that reduce metformin clearance:* Concomitant use of drugs that interfere with common renal tubular transport systems involved in the renal elimination of metformin (e.g., organic cationic transporter-2 [OCT2] / multidrug and toxin extrusion [MATE] inhibitors such as ranolazine, vandetanib, dolutegravir, and cimetidine) could increase systemic exposure to metformin. *Other:* Some drugs can adversely affect renal function which may increase the risk of lactic acidosis, e.g. NSAIDs, including selective cyclo-oxygenase (COX) II inhibitors, ACE inhibitors, angiotensin II receptor antagonists and diuretics, especially loop diuretics. When starting or using such products in combination with metformin-containing product, close monitoring of renal function is necessary. Certain drugs tend to cause hyperglycemia and may lead to loss of glycemic control. These drugs include the thiazides and other diuretics, corticosteroids, phenothiazines, thyroid products, estrogens, oral contraceptives, phenytoin, nicotinic acid, sympathomimetics, calcium channel blocking drugs, and isoniazid. There is an increased risk of lactic acidosis in acute alcohol intoxication (particularly in the case of fasting, malnutrition or hepatic impairment) due to metformin. Avoid consumption of alcohol and medicinal products containing alcohol.

ADVERSE REACTIONS: *Rare*: Hepatic dysfunction (including hepatitis), angioedema

MARKETED BY:

TORRENT PHARMACEUTICALS LTD.

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(Additional information is available on request)