STALIX M

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

Abbreviated Prescribing information for STALIX M (**Sitagliptin and metformin hydrochloride Tablets)** [Please refer the complete prescribing information for details]

PHARMACOLOGICAL PROPERTIES:

MECHANISM OF ACTION: Sitagliptin: Sitagliptin phosphate is an orally-active, potent, and highly selective inhibitor of the dipeptidyl peptidase 4 (DPP-4) enzyme for the treatment of type 2 diabetes. By inhibiting the DPP-4 enzyme, sitagliptin increases the levels of two known active incretin hormones, glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP). Metformin: Metformin is a biguanide with antihyperglycaemic effects, lowering both basal and postprandial plasma glucose. It does not stimulate insulin secretion and therefore does not produce hypoglycaemia. Metformin may act via three mechanisms:1) By reduction of hepatic glucose production by inhibiting gluconeogenesis and glycogenolysis 2) In muscle, by modestly increasing insulin sensitivity, improving peripheral glucose uptake and utilization 3) By delaying intestinal glucose absorption

INDICATIONS: A) FDC is indicated as triple combination therapy with a PPARy agonist (i.e a thiazolidinedione) as an adjunct to diet and exercise in patients inadequately controlled on their maximal tolerated dose of metformin and a PPARy agonist. B) FDC is also indicated as add-on to insulin (i.e triple combination therapy) as an adjunct to diet and exercise to improve glycemic control in patients when stable dosage of insulin and metformin alone do not provide adequate control.

DOSAGE AND ADMINISTRATION: The dose of Film-Coated STALIX M tablet should be individualised as directed by the Physician. Sitagliptin and metformin should be given twice daily with meals to reduce the gastrointestinal adverse reactions associated with metformin.

CONTRAINDICATION: Sitagliptin and metformin is contraindicated in patients with: hypersensitivity to the active substances or to any of the excipients, 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 the potential to alter renal function such as: dehydration, severe infection, shock, intravascular administration of iodinated contrast agents; acute or chronic disease which may cause tissue hypoxia such as: cardiac or respiratory failure, recent myocardial infarction, hepatic impairment; acute alcohol intoxication, alcoholism; breast-feeding.

WARNINGS & PRECAUTIONS Sitagliptin and metformin should not be used in patients with type 1 diabetes and must not be used for the treatment of diabetic ketoacidosis, Administration of iodinated contrast agent and Change in clinical status of patients with previously controlled type 2 diabetes. Acute pancreatitis: Use of DPP-4 inhibitors has been associated with a risk of developing acute pancreatitis. Lactic acidosis: Lactic acidosis, a rare but serious metabolic complication, most often occurs at acute worsening of renal function or cardiorespiratory illness or sepsis. Renal function: GFR should be assessed before treatment initiation and regularly thereafter Hypoglycaemia: Patients receiving Sitagliptin and metformin in combination with a sulphonylurea or with insulin may be at risk for hypoglycaemia. Hypersensitivity reactions, Bullous pemphigoid, Surgery: Sitagliptin and metformin must be discontinued at the time of surgery under general, spinal or epidural anaesthesia.

DRUG INTERACTIONS: Co-administration of multiple doses of sitagliptin (50 mg twice daily) and metformin (1,000 mg twice daily) did not meaningfully alter the pharmacokinetics of either sitagliptin or metformin in patients with type 2 diabetes. Concomitant use not recommended: Alcohol, Iodinated

contrast agents, Combinations requiring precautions for use: NSAIDs, Glucocorticoids, beta-2-agonists, diuretics, ACE-inhibitors, Effects of other medicinal products on sitagliptin: According to *In vitro* and clinical data described below suggest that the risk for clinically meaningful interactions following co-administration of other medicinal products is low.

ADVERSE REACTIONS: *Sitagliptin:* In reported monotherapy studies of sitagliptin 100 mg once daily alone compared to placebo, adverse reactions reported were headache, hypoglycaemia, constipation, and dizziness. Among these patients, adverse events reported regardless of causal relationship to medicinal product occurring in at least 5 % included upper respiratory tract infection and nasopharyngitis. In addition, osteoarthritis and pain in extremity were reported with frequency uncommon (> 0.5 % higher among sitagliptin users than that in the control group). *Metformin:* Gastrointestinal symptoms were reported very commonly in clinical studies and post-marketing use of metformin. Gastrointestinal symptoms such as nausea, vomiting, diarrhoea, abdominal pain and loss of appetite occur most frequently during initiation of therapy and resolve spontaneously in most cases. Additional adverse reactions associated with metformin include metallic taste (common); lactic acidosis, liver function disorders, hepatitis, urticaria, erythema, and pruritus (very rare). Long-term treatment with metformin has been associated with a decrease in vitamin. B12 absorption which may very rarely result in clinically significant vitamin B12 deficiency (e.g. megaloblastic anaemia).

MARKETED BY:

TORRENT PHARMACEUTICALS LTD.

IN/ STALIX M 50/500 mg and 850/ 1000 mg/MAR-22/01/ABPI

(Additional information is available on request)