Linaxa M XR

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

Abbreviated Prescribing information for **Linaxa M XR**

(Linagliptin And Metformin Hydrochloride Extended Release tablet 5 mg+ 1000 mg) [Please refer the complete prescribing information for details].

PHARMACOLOGICAL PROPERTIES:

Mechanism of Action:

Linagliptin: Linagliptin is an inhibitor of DPP-4, an enzyme that degrades the incretin hormones glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP). Thus, linagliptin increases the concentrations of active incretin hormones, stimulating the release of insulin in a glucose-dependent manner and decreasing the levels of glucagon in the circulation. Both incretin hormones are involved in the physiological regulation of glucose homeostasis. Incretin hormones are secreted at a low basal level throughout the day and levels rise immediately after meal intake. GLP-1 and GIP increase insulin biosynthesis and secretion from pancreatic beta cells in the presence of normal and elevated blood glucose levels. Furthermore, GLP-1 also reduces glucagon secretion from pancreatic alpha cells, resulting in a reduction in hepatic glucose output. *Metformin:* Metformin is an antihyperglycemic agent which improves glucose tolerance in patients with type 2 diabetes mellitus, 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. With metformin therapy, insulin secretion remains unchanged while fasting insulin levels and day-long plasma insulin response may actually decrease.

INDICATIONS: It is indicated as an adjunct to diet and exercise to improve glycaemic control in adult patients with type-II diabetes mellitus when treatment with Linagliptin and Metformin is appropriate.

DOSAGE AND ADMINISTRATION: As directed by the Physician.

CONTRAINDICATION: Severe renal impairment (eGFR below 30 mL/min/1.73 m), Acute or chronic metabolic acidosis, including diabetic ketoacidosis, Hypersensitivity to linagliptin, metformin, or any of the excipients in Linagliptin And Metformin Hydrochloride, reactions such as anaphylaxis, angioedema, exfoliative skin conditions, urticaria, or bronchial hyperreactivity have occurred with linagliptin.

WARNINGS & PRECAUTIONS:

Pancreatitis: Acute pancreatitis, including fatal pancreatitis, has been reported in patients treated with linagliptin. If pancreatitis is suspected, promptly discontinue Linagliptin And Metformin Hydrochloride. *Hypoglycemia with Concomitant Use with Insulin and Insulin Secretagogues:* Insulin secretagogues and insulin are known to cause hypoglycemia. The use linagliptin in combination with an insulin secretagogue (e.g., sulfonylurea) or insulin was associated with a higher rate of hypoglycemia compared with placebo in reported study. *Hypersensitivity Reactions:* There have been postmarketing reports of serious hypersensitivity reactions in patients treated with linagliptin. These reactions include anaphylaxis, angioedema, and exfoliative skin conditions. *Vitamin B Deficiency:* In metformin, reported study of 29-week duration, a decrease to subnormal levels of previously normal serum vitamin B levels was observed in approximately 7% of metformin-treated patients. *Severe and Disabling Arthralgia:* There have been postmarketing reports of severe and disabling arthralgia in patients taking DPP-4 inhibitors. Consider DPP-4 inhibitors as a possible cause for severe joint pain and discontinue drug if appropriate. *Bullous Pemphigoid:* Postmarketing cases of bullous pemphigoid requiring hospitalization

have been reported with DPP-4 inhibitor use. Linagliptin And Metformin Hydrochloride should be discontinued and referral to a dermatologist should be considered for diagnosis and appropriate treatment. *Heart Failure:* An association between DPP-4 inhibitor treatment and heart failure has been observed in cardiovascular outcomes trials for two other members of the DPP-4 inhibitor class. If heart failure develops, evaluate and manage according to current standards of care and consider discontinuation Linagliptin And Metformin Hydrochloride.

DRUG INTERACTIONS: *Carbonic Anhydrase Inhibitors:* Topiramate or other carbonic anhydrase inhibitors (e.g., zonisamide, acetazolamide or dichlorphenamide) frequently cause a decrease in serum bicarbonate and induce non-anion gap, hyperchloremic metabolic acidosis. *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 and may increase the risk for lactic acidosis. *Alcohol:* Alcohol is known to potentiate the effect of metformin on lactate metabolism. Intervention Warn patients against excessive alcohol intake while receiving Linagliptin And Metformin Hydrochloride. *Insulin or Insulin Secretagogues:* The use of linagliptin in combination with an insulin secretagogue (e.g., sulfonylurea) or insulin was associated with a higher rate of hypoglycemia compared with placebo in reported clinical trials. Metformin may increase the risk of hypoglycemia when combined with insulin and/or an insulin secretagogue. *Drugs Affecting Glycemic Control:* Certain drugs tend to produce 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. *Inducers of P-glycoprotein or CYP3A4 Enzymes:* Rifampin decreased linagliptin exposure, suggesting that the efficacy of linagliptin may be reduced when administered in combination with a strong P-gp or CYP3A4 inducer.

ADVERSE REACTIONS: Lactic Acidosis, Pancreatitis, Hypersensitivity Reactions, Vitamin B Deficiency, Severe and Disabling Arthralgia, Bullous Pemphigoid

MARKETED BY:

TORRENT PHARMACEUTICALS LTD.

Torrent House, Off Ashram Road,

Ahmedabad-380 009, INDIA

IN/Linaxa M XR 5 mg/1000 mg/Jun-23/01/ABPI

(Additional information is available on request)