

LINAXA EM

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

Abbreviated Prescribing information for LINAXA EM [Empagliflozin, Linagliptin and Metformin Hydrochloride ER Tablets (10 mg+5 mg +1000 mg) (25 mg+5 mg+1000 mg)]

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

PHARMACOLOGICAL PROPERTIES:

MECHANISM OF ACTION: *Empagliflozin* Empagliflozin is an inhibitor of the SGLT2, the predominant transporter responsible for reabsorption of glucose from the glomerular filtrate back into the circulation. By inhibiting SGLT2, empagliflozin reduces renal reabsorption of filtered glucose and lowers the renal threshold for glucose, and thereby increases urinary glucose excretion. *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). *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.

INDICATIONS: It is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Empagliflozin is indicated to reduce the risk of cardiovascular death in adults with type 2 diabetes mellitus and established cardiovascular disease.

DOSAGE AND ADMINISTRATION: **Recommended Dosage and Administration:**

Individualize the starting dosage of LINAXA EM based on the patient's current regimen:

- In patients on metformin HCl, with or without linagliptin, switch to LINAXA EM containing a similar total daily dosage of metformin HCl and a total daily dosage of empagliflozin 10 mg and linagliptin 5 mg.
- In patients on metformin HCl and any regimen containing empagliflozin, with or without linagliptin, switch to LINAXA EM containing a similar total daily dosage of metformin HCl, the same total daily dosage of empagliflozin and linagliptin 5 mg.
- Monitor effectiveness and tolerability, and adjust dosing as appropriate, not to exceed the maximum recommended daily dosage of empagliflozin 25 mg, linagliptin 5 mg and metformin HCl 2,000 mg.
- Take LINAXA EM orally, once daily with a meal in the morning.
 - Take LINAXA EM 10 mg/5 mg/1,000 mg or LINAXA EM 25 mg/5 mg/1,000 mg as a single tablet once daily.
- Swallow LINAXA EM tablets whole. Do not split, crush, dissolve, or chew.

CONTRAINDICATION: - Severe renal impairment (eGFR less than 30 mL/min/1.73 m²), end-stage renal disease, or dialysis - Acute or chronic metabolic acidosis, including diabetic ketoacidosis - Hypersensitivity to empagliflozin, linagliptin, metformin or any of the excipients in LINAXA EM, reactions such as anaphylaxis, angioedema, exfoliative skin conditions, urticaria, or bronchial hyperreactivity have occurred.

WARNINGS & PRECAUTIONS: Lactic acidosis Post marketing cases of metformin-associated lactic acidosis, including fatal cases, reported Lactic acidosis has a subtle onset and may be accompanied by nonspecific symptoms (eg, malaise, myalgias, abdominal pain, respiratory distress, increased

somnolence); however, hypothermia, hypotension, and resistant bradyarrhythmias have occurred with severe acidosis. Metformin-associated lactic acidosis characterized by elevated blood lactate concentrations (>5 mmol/L). Necrotizing Fasciitis of the Perineum (Fournier's Gangrene) Reports of necrotizing fasciitis of the perineum (Fournier's gangrene), a rare but serious and life-threatening necrotizing infection requiring urgent surgical intervention.

Hypoglycemia with Concomitant Use with Insulin and Insulin Secretagogues Insulin secretagogues and insulin are known to cause hypoglycemia. 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 study Lower Limb Amputation. In some clinical studies with SGLT2 inhibitors an imbalance in the incidence of lower limb amputation has been observed. 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. Pancreatitis Acute pancreatitis, including fatal pancreatitis, has been reported in patients treated with linagliptin. Vitamin B₁₂ Deficiency In metformin clinical trials of 29-week duration, a decrease to subnormal levels of previously normal serum vitamin B₁₂ 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 linagliptin. The time to onset of symptoms following initiation of drug therapy varied from one day to years. Bullous Pemphigoid Bullous pemphigoid was reported in 7 (0.2%) patients treated with linagliptin compared to none in patients treated with placebo in the CARMELINA trial and 3 of these patients were hospitalized due to bullous pemphigoid. 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.

DRUG INTERACTIONS: Topiramate or other carbonic anhydrase inhibitors, ranolazine, vandetanib, dolutegravir, and cimetidine, Alcohol, Diuretics, Insulin or Insulin Secretagogues, Drugs Affecting Glycemic Control, Lithium, Inducers of P-glycoprotein or CYP3A4 Enzymes, Positive Urine Glucose Test.

ADVERSE REACTIONS: Hypoglycemia with Concomitant Use with Insulin and Insulin Secretagogues, Necrotizing Fasciitis of the Perineum (Fournier's Gangrene), Genital Mycotic Infections, Lower Limb Amputation, Hypersensitivity Reactions, Vitamin B₁₂ Deficiency, Severe and Disabling Arthralgia, Bullous Pemphigoid, Heart Failure.

MARKETED BY:



TORRENT PHARMACEUTICALS LTD.

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(Additional information is available on request)