EMPAZIO M 12.5+500

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

Abbreviated Prescribing information for EMPAZIO M 12.5+500 [Empagliflozin and Metformin Hydrochloride Tablets 12.5 mg + 500 mg]
[Please refer the complete prescribing information available at www.torrentpharma.com]

PHARMACOLOGICAL PROPERTIES:
MECHANISM OF ACTION: EMPAZIO M contains: empagliflozin, a sodium-glucose co-transporter 2 (SGLT2) inhibitor, and metformin, a biguanide.
Empagliflozin: Sodium-glucose co-transporter 2 (SGLT2) is the predominant transporter responsible for reabsorption of glucose from the glomerular filtrate back into the circulation. Empagliflozin is an inhibitor of SGLT2. By inhibiting SGLT2, empagliflozin reduces renal reabsorption of filtered glucose and lowers the renal threshold for glucose, and thereby increases urinary glucose excretion.
Metformin HCl: Metformin is an antihyperglycemic agent which improves glucose tolerance in patients with type 2 diabetes mellitus, lowering both basal and postprandial plasma glucose. It is not chemically or pharmacologically related to any other classes of oral antihyperglycemic agents. Metformin decreases hepatic glucose production, decreases intestinal absorption of glucose, and improves insulin sensitivity by increasing peripheral glucose uptake and utilization. Unlike SUs, metformin does not produce hypoglycemia in either patients with type 2 diabetes mellitus or normal subjects (except in special 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 as an adjunct to diet and exercise to improve glycemic control in adult patients with type 2 diabetes mellitus who are not adequately controlled on a regimen containing empagliflozin or Metformin, or in patients already being treated with both empagliflozin and Metformin.

DOSAGE AND ADMINISTRATION: *Prior to Initiation of EMPAZIO M* : Assess renal function before initiating EMPAZIO M and as clinically indicated. In patients with volume depletion, correct this condition before initiating EMPAZIO M. *Recommended Dosage and Administration*: Individualize the starting dose of EMPAZIO M based on the patient's current regimen: In patients on metformin hydrochloride (HCl), switch to EMPAZIO M containing empagliflozin 5 mg with a similar total daily dose of metformin HCl;

- In patients on empagliflozin, switch to EMPAZIO M containing metformin HCl 500 mg with a similar total daily dose of empagliflozin.
- In patients already treated with empagliflozin and metformin HCl, switch to EMPAZIO M containing the same total daily doses of each component.
- In patients with volume depletion, correct this condition before initiating EMPAZIO M
- Monitor effectiveness and tolerability, and adjust dosing as appropriate, not to exceed the maximum recommended daily dose of empagliflozin 25 mg and metformin HCl 2000 mg.
- Take EMPAZIO M twice daily with meals; with gradual dose escalation to reduce the gastrointestinal side effects due to metformin.

Method of administration*:* Oral use. The tablet should be swallowed whole and never crushed, cut, or chewed.

CONTRAINDICATION: ***a)*** Severe renal impairment (eGFR below 30 mL/min/1.73 m2), end stage renal disease, or on dialysis. ***b)*** Acute or chronic metabolic acidosis, including diabetic ketoacidosis. ***c)*** Hypersensitivity to empagliflozin, metformin or any of the formulation excipients in this FDC product.

WARNINGS & PRECAUTIONS: ***Lactic acidosis:*** There have been postmarketing cases of metformin-associated lactic acidosis, including fatal cases. These cases had a subtle onset and were accompanied by nonspecific symptoms such as malaise, myalgias, abdominal pain, respiratory distress, or increased somnolence; however, hypothermia, hypotension, and resistant bradyarrhythmias have occurred with severe acidosis. ***Diabetic ketoacidosis:*** Reports of ketoacidosis, a serious life-threatening condition requiring urgent hospitalization have been identified in clinical trials and postmarketing surveillance in patients with type 1 and type 2 diabetes mellitus receiving sodium glucose co-transporter-2 (SGLT2) inhibitors, including empagliflozin. ***Urosepsis and Pyelonephritis*:** There have been

postmarketing reports of serious urinary tract infections including urosepsis and pyelonephritis requiring hospitalization in patients receiving SGLT2 inhibitors, including empagliflozin. *Hypoglycemia with Concomitant Use with Insulin and Insulin Secretagogues*: Insulin and insulin secretagogues are known to cause hypoglycemia. ***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, have been identified in postmarketing surveillance in patients with diabetes mellitus receiving SGLT2 inhibitors, including empagliflozin***. Genital Mycotic Infections***: Empagliflozin increases the risk for genital mycotic infections. ***Hypersensitivity Reactions***: There have been postmarketing reports of serious hypersensitivity reactions, (e.g., angioedema) in patients treated with empagliflozin. ***Vitamin B12 Deficiency*:** In metformin clinical trials of 29-week duration, a decrease to subnormal levels of previously normal serum vitamin B_{12} levels was observed in approximately 7% of metformin-treated patients.

DRUG INTERACTIONS: ***Carbonic Anhydrase Inhibitors*:** Topiramate or other carbonic anhydrase inhibitors. ***Drugs that Reduce Metformin Clearance***: Concomitant use of drugs that interfere with common renal tubular transport systems involved in the renal elimination of metformin. ***Alcohol*:** Warn patients against excessive alcohol intake while receiving EMPAZIO M. ***Diuretics***: Coadministration of empagliflozin with diuretics resulted in increased urine volume and frequency of voids. ***Insulin or Insulin Secretagogues***: The risk of hypoglycemia is increased when empagliflozin is used in combination with insulin secretagogues. Drugs Affecting Glycemic Control: Certain drugs tend to produce hyperglycemia and may lead to loss of glycemic control. Positive Urine Glucose Test: SGLT2 inhibitors increase urinary glucose excretion and will lead to positive urine glucose tests. ***Interference with 1,5-anhydroglucitol (1,5-AG) Assay:*** Measurements of 1,5-AG are unreliable in assessing glycemic control in patients taking SGLT2 inhibitors.

ADVERSE REACTIONS: Lactic Acidosis, Ketoacidosis, Volume Depletion, Urosepsis and Pyelonephritis, Hypoglycemia with Concomitant Use with Insulin and Insulin Secretagogues, Necrotizing Fasciitis of the Perineum (Fournier's Gangrene), Genital Mycotic Infections, Hypersensitivity Reactions, Vitamin B12 Deficiency.

MARKETED BY:

Torrent Pharmaceuticals Limited.

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(Additional information is available on request)