8.0 cm

13 cm

Ligazid® MX

Linagliptin INN and Metformin Hydrochloride BP

Extended Release Tablet

Ligazid® MX is a combined preparation of Linagliptin and Metformin Hydrochloride. This combination combines 2 antihyperglycemic agents with complementary mechanisms of action to improve glycemic control in patients with type 2 diabetes mellitus: Linagliptin, a dipeptidyl peptidase-4 (DPP-4) inhibitor, and Metformin, a member of the biguanide class. 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 is an antihyperglycemic agent which improves glucose tolerance in patients with type 2 diabetes mellitus, lowering both basal and postprandial plasma glucose. Its pharmacologic mechanisms of action are different from 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

Indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both Linagliptin and Metformin is appropriate.

DOSAGE AND ADMINISTRATION

The dosage of Linagliptin and Metformin Hydrochloride ER tablet should be individualized on the basis of both effectiveness and tolerability, while not exceeding the maximum recommended total daily dose of linagliptin 5 mg and metformin Hydrochloride 2000 mg. Linagliptin and Metformin Hydrochloride should be given once daily with a meal.

Recommended starting dose:

• In patients currently not treated with Metformin, initiate Linagliptin and Metformin Hydrochloride ER tablet treatment with 5 mg Linagliptin/1000 mg Metformin Hydrochloride extended-release once daily with a meal.
• In patients already treated with Metformin, start Linagliptin and Metformin Hydrochloride ER tablet with 5 mg of Linagliptin total daily dose and a similar total daily dose of Metformin Hydrochloride once daily with a meal.
• In patients already treated with Linagliptin and Metformin or Linagliptin and Metformin Hydrochloride ER tablet, switch to Linagliptin and Metformin Hydrochloride ER tablet containing 5 mg of Linagliptin total daily dose and a similar total daily dose of Metformin Hydrochloride once daily with a meal.

Linagliptin and Metformin Hydrochloride ER tablet should be swallowed whole. The tablets must not be split, crushed, dissolved or chewed.

Linagliptin and Metformin Hydrochloride ER tablet should be taken as a single tablet once daily. Patients using 2.5 mg Linagliptin/1000 mg Metformin Hydrochloride ER tablets should take two tablets together once daily.

CONTRAINDICATIONS

• Severe renal impairment (eGFR below 30 mL/min/1.73 m2) • Metabolic acidosis, including diabetic ketoacidosis • History of hypersensitivity reaction to linagliptin, such as anaphylaxis, angioedema, exfoliative skin conditions, urticaria, or bronchial hyperreactivity • Hypersensitivity to metformin

SIDE EFFECTS

• Nasopharyngitis and diarrhea • Heart Failure • Pancreatitis

ADVERSE REACTIONS

The following serious adverse reactions are described below or elsewhere in the prescribing information:
• Lactic Acidosis • Pancreatitis • Use with Medications Known to Cause Hypoglycemia • Hypersensitivity Reactions • Vitamin B_{12} Deficiency • Severe and Disabling Arthralgia • Bullous Pemphigoid • Heart Failure

PRECAUTION AND WARNING

Lactic acidosis: Warn against excessive alcohol use. This combination is not recommended in hepatic impairment or hypoxic states and is contraindicated in renal impairment. Ensure normal renal function before initiating and at least annually thereafter. Hypoglycemia: When used with a sulfonylurea, a lower dose of the sulfonylurea may be required to reduce the risk of hypoglycemia. Vitamin B12 deficiency: Metformin may lower vitamin B12 levels. Monitor hematologic parameters annually.

USE IN PREGNANCY AND LACTATION

Pregnancy Category B. There are no adequate and well controlled studies in pregnant women with this combination or its individual components, and some clinical data is available for Metformin which indicate that the risk for major malformations was not increased when Metformin is taken during the first trimester in pregnancy. In addition, Metformin was not associated with increased perinatal complications. Nevertheless, because these clinical data cannot rule out the possibility of harm, this combination should be used during pregnancy only if clearly needed.

It is not known whether Linagliptin is excreted in human milk. Metformin is excreted in human milk in low concentrations. Because the potential for hypoglycemia in nursing infants may exist, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

PHARMACEUTICAL PRECAUTION

Do not store above 30 °C temperature. Keep away from light and wet place. Keep out of reach of children.

PACKAGING

Ligazid® MX Extended Release Tablet:

Box containing 3 strips of 6 tablets each. Each extended release tablet contains Linagliptin INN 5 mg and Metformin Hydrochloride BP 1000 mg.

SK+F
Manufactured by
ESKAYEF PHARMACEUTICALS LTD.
TONGI, GAZIPUR, BANGLADESH.

PM09133 V01

PM Specification

Job Name	**: Ligazid MX Extended Release Tablet Insert**	Paper	: 60 gsm offset paper
Size	: L - 13.0 cm, W - 8.0 cm	Lamination	: N/A
Print	: 1 Color	Loading Process	: N/A
Pantone Code: ■ PANTONE 419 C		Others	:

CSD 04 UZL