

# Linaglip-M

Linagliptin INN & Metformin Hydrochloride BP

## COMPOSITION:

**Linaglip-M 2.5/500 Tablet:** Each film coated tablet contains Linagliptin INN 2.5 mg & Metformin Hydrochloride BP 500 mg.

**Linaglip-M 2.5/850 Tablet:** Each film coated tablet contains Linagliptin INN 2.5 mg & Metformin Hydrochloride BP 850 mg.

**Linaglip-M 2.5/1000 Tablet:** Each film coated tablet contains Linagliptin INN 2.5 mg & Metformin Hydrochloride BP 1000 mg.

**Linaglip-M 5/1000 ER Tablet:** Each film coated tablet contains Linagliptin INN 5 mg & Metformin Hydrochloride BP 1000 mg extended-release.

## PHARMACOLOGY:

Linaglip-M combines 2 antihyperglycemic agents Linagliptin, (a DPP-4 inhibitor) & Metformin (a biguanide) with complementary mechanisms of action to improve glycemic control in patients with type 2 diabetes mellitus. Linagliptin inhibits DPP-4 enzyme so that incretin hormone (GLP-1 & GIP) keeps safe from degradation & its concentration increases in circulation where GLP-1 & GIP increase the insulin production in glucose dependent manner & reduces hepatic glucose output. Thus, it controls blood sugar in blood. Metformin lowers both basal and postprandial plasma glucose. Metformin may exert its glucose-lowering effect via four mechanisms:- by reduction of hepatic glucose production through inhibition of gluconeogenesis and glycogenolysis; - in muscle, by modestly increasing insulin sensitivity, improving peripheral glucose uptake and utilization; - by delaying intestinal glucose absorption; - stimulate intracellular glycogen synthesis by acting on glycogen synthase and increase the transport capacity of glucose transporters (GLUT-1 & GLUT-4).

## INDICATIONS:

**Linaglip-M** is 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. Combination of Linagliptin and Metformin is not recommended for treatment of type 1 diabetes or diabetic ketoacidosis and has not been studied in patients with a history of pancreatitis.

## DOSAGE AND ADMINISTRATION:

Recommended starting dose for 2.5/500, 2.5/850 & 2.5/1000 mg tablet:

- Patients not currently treated with Metformin: Initiate treatment with **Linaglip-M 2.5/500** tablet twice daily.
- Patients already treated with Metformin: If patient is taking Metformin 500 mg tablet twice daily, then give him/her **Linaglip-M 2.5/500** tablet twice daily. If patient is taking Metformin 850 mg tablet twice daily, then give him/her **Linaglip-M 2.5/850** tablet twice daily.
- Patients already treated with Linagliptin and Metformin individual components: May be switched to **Linaglip-M** containing the same doses of each component
- Maximum recommended dose is **Linaglip-M 2.5/1000** tablet twice daily.

Recommended starting dose for 5/1000 mg ER tablet:

- In patients currently not treated with metformin: Initiate **Linaglip-M 5/1000 ER** tablet once daily with a meal
- In patients already treated with metformin: Start **Linaglip-M 5/1000 ER** tablet once daily with a meal
- In patients already treated with Linagliptin and Metformin or their combination: May be switched to **Linaglip-M 5/1000 ER** tablet once daily with a meal containing the same doses of each component

## CONTRAINDICATIONS:

This combination of Linagliptin & Metformin is contraindicated in patients with renal impairment (e.g., serum creatinine >1.5 mg/dL for men, >1.4 mg/dL for women, or abnormal creatinine clearance). This combination is also contraindicated in case of acute or chronic metabolic acidosis, diabetic ketoacidosis, hypersensitivity reaction to Linagliptin or

metformin.

## WARNINGS AND PRECAUTIONS:

If the patient experiences hypoglycemia with others secretagogues or any incident of lactic acidosis, or hypersensitivity to Linagliptin/Metformin then discontinue the medications.

## SIDE EFFECTS:

The most common side effects of Linagliptin & Metformin combination are weakness or tiredness, unusual muscle pain, nausea, vomiting, diarrhea, dizziness, nasopharyngitis etc.

## USE IN PREGNANCY & LACTATION:

Pregnancy: Linagliptin & Metformin combination is pregnancy Category B. Linagliptin & Metformin combination tablets should be used during pregnancy only if clearly needed. But the limited data with combination of Linagliptin & Metformin combination extended release tablet use in pregnant women are not sufficient to inform a Linagliptin & Metformin extended-release combination - associated or Linagliptin - associated risk for major birth defects and miscarriage.

Nursing mothers: There is no information regarding the presence of both Linagliptin & Metformin combination and Linagliptin & Metformin combination extended release tablet or Linagliptin in human milk, the effects on the breastfed infant, or the effects on milk production.

## USE IN CHILDREN & ADOLESCENTS:

Safety and effectiveness of Linagliptin & Metformin combination in pediatric patients under 18 years of age have not been established.

## DRUG INTERACTIONS:

Drug Interactions with Metformin: some drugs can interact with metformin like- digoxin, amiloride, procainamide, quinidine, quinine, ranitidine, trimethoprim, vancomycin, topiramate, acetazolamide, alcohol; so caution & proper patient monitoring is required.

Drug Interactions with Linagliptin: some drugs can interact also with Linagliptin like- Rifampin, P-gp, thiazide diuretics, corticosteroids, phenothiazines, thyroid products, phenytoin, nicotinic acid, etc. so caution & proper patient monitoring is required.

## OVERDOSE:

Linagliptin

During controlled clinical trials in healthy subjects, with single doses of up to 600 mg of Linagliptin, there were no dose-related clinical adverse drug reactions. There is no experience with doses above 600 mg in humans.

Metformin

Overdose of Metformin has occurred, including ingestion of amounts greater than 50 grams. Hypoglycemia was reported in approximately 10% of cases, but no causal association with Metformin has been established. Lactic acidosis has been reported in approximately 32% of Metformin overdose cases.

## STORAGE:

- **Linaglip-M 2.5/500, 2.5/850 & 2.5/1000 Tablet:** Store below 30°C, keep in dry place & protect from light.
- **Linaglip-M 5/1000 ER Tablet:** Store below 25°C, keep in dry place & protect from light.
- Keep out of the reach of children.

## PACKING:

**Linaglip-M 2.5/500 Tablet:** Each box contains 30 tablets in alu-alu blister pack.

**Linaglip-M 2.5/850 Tablet:** Each box contains 30 tablets in alu-alu blister pack.

**Linaglip-M 2.5/1000 Tablet:** Each box contains 30 tablets in alu-alu blister pack.

**Linaglip-M 5/1000 ER Tablet:** Each box contains 28 tablets in alu-alu blister pack.

Manufactured by:

 **ARISTOPHARMA LTD.**  
Shampur-Kadamtali I/A, Dhaka-Bangladesh