Linadus® M

Linagliptin & Metformin HCl

Descriptions: Linadus® M is a combination of Linagliptin & Metformin Hydrochloride, two oral antihyperglycemic drugs with complimentary mechanism of action. Linagliptin is a Dipeptidyl Peptidase-4 (DPP-4) inhibitor and Metformin is a member of the biguanide class.

Mode of Action: Linagliptin is a dipeptidyl peptidase-4 (DPP-4) inhibitor, which exerts its action by slowing the inactivation of incretin hormones. Incretin hormone levels are increased in response to a meal. When blood glucose concentrations are normal or elevated, incretin hormones increase insulin synthesis and releases insulin from pancreatic beta cells. Incretin hormones also lowers glucagon secretion from pancreatic alpha cells, leading to reduced hepatic glucose production.
Metformin decreases hepatic glucose production, decreases intestinal absorption of glucose, and increases peripheral glucose uptake and utilization.

Pharmacokinets: Linagliptin is rapidly absorbed and the peak plasma concentration occur between 1.5 hours. The absolute bioavailability is approximately 30%. 70%-80% is protein bound. It is not extensively metabolized, 90% of dose excreted unchanged. It is eliminated via the feces 80% & urine 5%.
The absolute bioavailability of metformin at fasting condition is approximately 50-60%. Food decreases the extent & slightly delays the absorption of metformin. Metformin is negligible bound to plasma proteins in contrast to sulfonylureas. The elimination half-life is approximately 17.6 hours.

Composition: Linadus® M 2.5/500 Tablet: Each film coated tablet contains Linagliptin INN 2.5 mg and Metfromin Hydrochloride USP 500 mg.
Linadus® M 2.5/850 Tablet: Each film coated tablet contains Linagliptin INN 2.5 mg and Metfromin Hydrochloride USP 850 mg.
Linadus® M 2.5/1000 Tablet: Each film coated tablet contains Linagliptin INN 2.5 mg and Metfromin Hydrochloride USP 1000 mg.

Indication: Linadus® 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.

Dosage & administration: The dosage of **Linadus® M** should be individualized on the basis of both effectiveness and tolerability. Maximum recommended dose is 2.5 mg Linagliptin and 1000 mg Metformin Hydrochloride twice daily with meals. Dose escalation should be gradual to reduce the gastrointestinal (GI) side effects associated with Metformin use.
Recommended starting dose: In patients currently not treated with Metformin, initiate treatment with 2.5 mg Linagliptin and 500 mg Metformin Hydrochloride twice daily.
In patients already treated with Metformin, start with 2.5 mg Linagliptin and the current dose of Metformin Hydrochloride twice daily. Patients already treated with linagliptin and metformin, individual components may be switched to this combination containing the same doses of each component.

Contraindication: Linagliptin and Metformin combination is contraindicated in patients with renal impairment. It is also contraindicated in acute or chronic metabolic acidosis (diabetic ketoacidosis) and in hypersensitivity to Linagliptin or Metformin.

Side Effects: ● Nasopharyngitis ● Diarrhea ● Hypoglycemia

Use in pregnancy & lactation: *Pregnancy:* Pregnancy category B. There are no adequate and well-controlled studies in pregnant women. Linagliptin + Metformin combination tablets should be used during pregnancy only if clearly needed.
Lactation: Caution should be exercised when Linagliptin + Metformin combination is administered to a nursing woman.

Precaution: In a patient with lactic acidosis who is taking Metformin, the drug should be discontinued immediately and supportive therapy promptly instituted. There have been postmarketing reports of acute pancreatitis. If pancreatitis is suspected, promptly discontinue **Linadus® M**. Temporarily discontinue **Linadus® M** in patients undergoing radiologic studies with intravascular administration of iodinated contrast materials or any surgical procedures necessitating restricted intake of food and fluids. Metformin may lower Vitamin B12 levels; so hematologic parameters should be monitored annually.

Drug interaction: Cationic drugs (amiloride, digoxin, morphine, ranitidine, trimethoprim etc.): May reduce metformin elimination. P-glycoprotien/CYP3A4 inducer (i.e. rifampin): The efficacy of **Linadus® M** may be reduced when administered in combination.
Overdose: *Linagliptin:* During controlled clinical trials in healthy subjects, with single doses of up to 600 mg of Linagliptin (equivalent to 120 times the recommended daily dose), 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: Store in a cool (below 25˚C temperature) and dry place protected from light.

Packaging: Linadus® M 2.5/500 Tablet: Each carton contains 10X3 tablets in Alu-Alu blister pack.
Linadus® M 2.5/850 Tablet: Each carton contains 6X3 tablets in Alu-Alu blister pack.
Linadus® M 2.5/1000 Tablet: Each carton contains 6X3 tablets in Alu-Alu blister pack.