Only for the use of Medical Professionals

Glitin M®

Linagliptin + Metformin

Description

Glitin M® is the preparation of Linagliptin and Metformin. Linagliptin is an inhibitor of dipeptidyl peptidase-4 (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 decreases hepatic glucose production, decreases intestinal absorption of glucose and improves insulin sensitivity by increasing peripheral glucose uptake and utilization.

Indications

Glitin 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.

Important limitations of use

• Not for treatment of type 1 diabetes or diabetic ketoacidosis.

• Has not been studied in combination with insulin.

Dosage and administration

Adult: The dosage of **Glitin M®** should be individualized on the basis of both effectiveness and tolerability, while not exceeding the maximum recommended dose of 2.5 mg linagliptin/1000 mg metformin twice daily. **Glitin M®** should be given twice daily with meals. Dose escalation should be gradual to reduce the gastrointestinal (GI) side effects associated with metformin use. The recommended starting doses are given below:

• In patients currently not treated with metformin, initiate treatment with 2.5 mg linagliptin/500 mg metformin twice daily.

• In patients already treated with metformin, start with 2.5 mg linagliptin and the current dose of metformin taken at each of the two daily meals.

• Patients already treated with linagliptin and metformin individual components may be switched to **Glitin M®** containing the same doses of each component.

Concomitant use with sulfonylurea: When **Glitin M®** is used in combination with an insulin secretagogue (e.g., sulfonylurea), a lower dose of the insulin secretagogue may be required to reduce the risk of hypoglycemia.
Children: Safety and effectiveness of this combination in children under 18 years of age have not been established.

Use in pregnancy and lactation
Pregnancy: Linagliptin and metformin combination is pregnancy category B drug. There are no adequate and well-controlled studies in pregnant women. This combination should be used during pregnancy only if clearly needed.
Lactation: 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.

Side effects
The side effects of linagliptin and metformin combination are diarrhea, nasopharyngitis, hypoglycemia and pancreatitis.

Contraindications
Linagliptin and metformin combination is contraindicated in patients with known hypersensitivity to linagliptin or metformin or any components of this product. This combination is also 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) and acute or chronic metabolic acidosis, including diabetic ketoacidosis.

Warnings and precautions
Lactic acidosis can occur due to metformin accumulation. The risk increases with conditions such as renal impairment, sepsis, dehydration, excess alcohol intake, hepatic impairment, and acute congestive heart failure. Ensure normal renal function before initiating and at least annually thereafter. Temporarily discontinue this combination 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. Monitor hematologic parameters annually.

Drug interactions
Cationic drugs (e.g., digoxin, morphin) that are eliminated via the proximal renal tubular system may interact with metformin. So, careful patient monitoring and dose adjustment of linagliptin and metformin combination or interfering drugs is recommended in patients taking cationic medications. Use carbonic anhydrase inhibitors (e.g., topiramate) with caution in patients treated with linagliptin and metformin combination, as the risk of lactic acidosis may increase. The efficacy of linagliptin may be reduced when administered in

combination with a strong P-glycoprotein or CYP3A4 inducer (e.g., rifampin). Use of alternative treatments (not containing linagliptin) is strongly recommended.

Overdose

In the event of an overdose with linagliptin and metformin combination, employ the usual supportive measures as dictated by the patient's clinical status. Removal of linagliptin by hemodialysis or peritoneal dialysis is unlikely. However, metformin is dialyzable with a clearance of up to 170 ml/min under good hemodynamic conditions. Therefore, hemodialysis may be useful partly for removal of accumulated metformin from patients in whom linagliptin and metformin combination overdose is suspected.

Pharmaceutical precautions

Store in a cool (below 25o C) & dry place protected from light. Keep away from the reach of children.

Presentation

Glitin M® 2.5/500 tablet: Each coated tablet contains Linagliptin INN 2.5 mg and Metformin Hydrochloride BP 500 mg.
Glitin M® 2.5/850 tablet: Each coated tablet contains Linagliptin INN 2.5 mg and Metformin Hydrochloride BP 850 mg.
Glitin M® 2.5/1000 tablet: Each coated tablet contains Linagliptin INN 2.5 mg and Metformin Hydrochloride BP 1000 mg.

Package quantity

Glitin M® 2.5/500 tablet: Carton of 30 tablets in a blister pack.
Glitin M® 2.5/850 tablet: Carton of 30 tablets in a blister pack.
Glitin M® 2.5/1000 tablet: Carton of 20 tablets in a blister pack
® Registered Trade Mark

ACI Limited
Godnyl, Narayanganj, Bangladesh