Liglimet™

Linagliptin and Metformin

COMPOSITION

Liglimet™ 2.5/500: Each tablet contains Linagliptin INN 2.5 mg and Metformin Hydrochloride BP 500 mg.
Liglimet™ 2.5/850: Each tablet contains Linagliptin INN 2.5 mg and Metformin Hydrochloride BP 850 mg.
Liglimet™ **XR** 5/1000: Each extended release tablet contains Linagliptin INN 5 mg and Metformin Hydrochloride EP 1000 mg.

PHARMACOLOGY

Liglimet™ combines two antihyperglycemic agents with complementary mechanisms of action to improve glycemic control in patients with type 2 diabetes: Linagliptin, a dipeptidyl peptidase-4 (DPP-4) inhibitor, and Metformin Hydrochloride, a member of the biguanide class.

Linagliptin is a dipeptidyl peptidase-4 (DPP-4) inhibitor, which is believed to exert its actions in patients with type 2 diabetes by slowing the inactivation of incretin hormones. Incretin hormones, including glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP), are released by the intestine throughout the day, and levels are increased in response to a meal. These hormones are rapidly inactivated by the enzyme, DPP-4. The incretins are part of an endogenous system involved in the physiologic regulation of glucose homeostasis. When blood glucose concentrations are normal or elevated, GLP-1 and GIP increase insulin synthesis and release from pancreatic beta cells by intracellular signaling pathways involving cyclic AMP. GLP-1 also lowers glucagon secretion from pancreatic alpha cells, leading to reduced hepatic glucose production. By increasing and prolonging active incretin levels, Linagliptin increases insulin release and decreases glucagon levels in the circulation in a glucose-dependent manner.

The pharmacologic mechanism of action of Metformin is different from other classes of oral antihyperglycemic agents. Metformin decreases hepatic glucose production, decreases intestinal absorption of glucose, and increases peripheral glucose uptake and utilization.

INDICATION AND USAGE

Liglimet™ 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 AND ADMINISTRATION

Dose of this combination should be individualized on the basis of the patient's current regimen, effectiveness, and tolerability while not exceeding the maximum recommended daily dose of 2.5 mg Linagliptin and 1000 mg Metformin twice daily.

Linagliptin/Metformin combination should generally be given twice daily with meals, with gradual dose escalation, to reduce the gastrointestinal (GI) side effects due to Metformin.

The recommended starting dose in patients currently not treated with Metformin, initiate treatment with 2.5 mg Linagliptin/500 mg Metformin Hydrochloride twice daily. The recommended starting dose 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.

The starting dose in Patients already treated with Linagliptin and Metformin individual components may be switched to Liglimet containing the same doses of each component.

For **Liglimet**™ **XR**

Recommended starting dose:

* In patients currently not treated with Metformin, initiate treatment with 5 mg Linagliptin/1000 mg Metformin Hydrochloride extended release once daily with a meal.
* In patients already treated with metformin, start with 5 mg of Linagliptin total daily dose and a similar total daily dose of Metformin once daily with a meal.
* In patients already treated with **Liglimet**™, switch to **Liglimet**™ **XR** containing 5 mg of Linagliptin total daily dose and a similar total daily dose of Metformin once daily with a meal.

Liglimet™ **XR** should be taken once daily where total daily dose should not exceed Linagliptin 5 mg and Metformin Hydrochloride 2000 mg. **Liglimet**™ **XR** should be swallowed whole. The tablets must not be split, crushed, dissolved, or chewed before swallowing.

CONTRAINDICATIONS

Linagliptin and Metformin is contraindicated in patients with:

* Severe renal impairment (eGFR below 30 ml/min/1.73 m^2)
* Acute or chronic metabolic acidosis, including diabetic ketoacidosis
* A history of hypersensitivity reaction to Linagliptin or Metformin

ADVERSE EFFECTS

Most common side effects are nasopharyngitis and diarrhea. Hypoglycemia is more common in patients treated with this combination and sulfonylureas.

DRUG INTERACTION

Cationic drugs (amiloride, digoxin, morphine, ranitidine, trimethoprim etc.) may reduce Metformin elimination. P-glycoprotein/CYP3A4 inducer (i.e. rifampin): The efficacy of Linagliptin and Metformin may be reduced when administered in combination.

USE IN PREGNANCY & LACTATION

PREGNANCY: There are no adequate and well controlled studies in pregnant women with the combination of Metformin/Linagliptin or its individual components; therefore, the safety of the combination in pregnant women is not known. The combination of Linagliptin & Metformin should be used during pregnancy only if clearly needed.

NURSING MOTHERS: It is not known whether Linagliptin is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when **Liglimet**™ is administered to a nursing woman.

GERIATRIC USE: Linagliptin is minimally excreted by the kidney; however, metformin is substantially excreted by the kidney, and because aging can be associated with reduced renal function, **Liglimet**™ should be used with caution as age increases.

PEDIATRIC USE: Safety and effectiveness of Linagliptin/Metformin in pediatric patients under 18 years of age have not been established

STORAGE

Keep away from light. Store below 30°C. Keep out of the reach of the children.

HOW SUPPLIED

Liglimet™ 2.5/500: Each box contains 18's tablets in blister pack.
Liglimet™ 2.5/850: Each box contains 18's tablets in blister pack.
Liglimet™ **XR** 5/1000: Each box contains 20's tablets in blister pack.

Manufactured by:
SQUARE
PHARMACEUTICALS LTD.
Kaliakoir, Gazipur, Bangladesh

TM - Trade Mark

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