Linera 5

Linagliptin INN 5 mg

Composition
Linera 5: Each film-coated tablet contains Linagliptin INN 5 mg.

Pharmacology
Linagliptin inhibits DPP-4 enzyme which declines the incretin hormones glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP). Linagliptin increases the concentrations of active incretin hormones, stimulating the release of insulin in a glucose-dependent manner and decreasing the levels of glucagon. 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.

Indication and Usage
Linera 5 is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type-2 diabetes mellitus. **Linera 5** should not be used in patients with type-1 diabetes or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings. **Linera 5** has not been studied in combination with insulin.

Dosage and Administration
The recommended dose of **Linera 5** is 5 mg once daily and can be taken with or without food. If a dose is missed, it should be taken as soon as the patient remembers. A double dose should not be taken on the same day. For patients with renal insufficiency no dosage adjustment is required. Pharmacokinetic studies suggest that no dose adjustment is required for patients with hepatic impairment. When linagliptin is added to metformin, the dose of metformin should be maintained, and linagliptin administered concomitantly. When linagliptin is used in combination with a sulphonylurea or with insulin, a lower dose of the sulphonylurea or insulin, may be considered to reduce the risk of hypoglycemia.

Contraindication
Linera 5 is contraindicated in patients with a history of a hypersensitivity reaction to linagliptin, such as urticaria, angioedema, or bronchial hyperreactivity.

Warning and Precaution
* *Use with Medications Known to Cause Hypoglycemia:* Insulin secretagogues are known to cause hypoglycemia. The use of **Linera 5** in combination with an insulin secretagogue (e.g., sulfonylurea) was associated with a higher rate of hypoglycemia compared with placebo in clinical trial. Therefore, a lower dose of the insulin secretagogue may be required to reduce the risk of hypoglycemia when used in combination with **Linera 5**.
* *Macrovascular Outcomes:* There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with **Linera 5** tablets or any other antidiabetic drug.

Side Effect
The most common side effects of linagliptin are stuffy or runny nose and sore throat. Hypoglycemia may occur when **Linera 5** is combined with insulin or sulphonylurea and metformin. Allergic reaction and muscle pain also may occur. Pancreatitis, angioedema (frequency rare) and urticaria (frequency rare) were identified as additional adverse reactions.

Use in Pregnancy and Lactation
Pregnancy Category B. The use of linagliptin has not been studied in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of linagliptin during pregnancy. Available animal data have shown excretion of linagliptin in milk at a milk-to-plasma ratio of 4:1. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when **Linera 5** is administered to a nursing woman.

Use in Children and Adolescents
The safety and effectiveness of **Linera 5** in children and adolescents has not yet been established.

Drug Interaction
The efficacy of **Linera 5** may be reduced when administered in combination with a strong CYP3A4 inducer or P-glycoprotein inhibitor (e.g. rifampicin). Therefore, use of alternative treatments is strongly recommended when linagliptin is to be administered with CYP3A4 inducer or P-glycoprotein inhibitor. Sulfonylureas should be used with caution during treatment with linagliptin. The pharmacokinetic characteristics of linagliptin were not altered by the concomitant administration of simvastatin, digoxin, glyburide, warfarin, metformin or pioglitazone.

Overdose
During controlled clinical trials in healthy subjects, with single doses of up to 600 mg of **Linera 5** (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. It is also reasonable to employ the usual supportive measures, e.g., remove unabsorbed material from the gastrointestinal tract, employ clinical monitoring, and institute supportive treatment as dictated by the patient's clinical status. Linagliptin is not expected to be eliminated to a therapeutically significant degree by hemodialysis or peritoneal dialysis.

Storage
Do not store above 25ºC. Protect from light. Keep all medicines out of the reach of children.

Packaging
Linera 5: Each box contains 3x10's tablets in blister pack.

Manufactured by
ZISKA PHARMA
Ziska Pharmaceuticals Ltd.
Kaliakoir, Gazipur, Bangladesh