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LINA®

(Linagliptin)

Tablet

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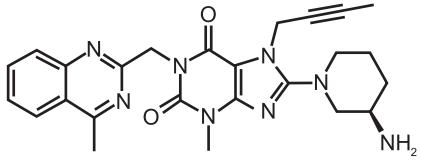
COMPOSITION:
Each film coated tablet contains:
Linagliptin ..... 5 mg.

Product Specs.: Innovator

INTRODUCTION:
Linagliptin is described chemically as 1H-Purine-2,6-dione, 8-[(3R)-3-amino-1-piperidinyl]-7-(2-butyn-1-yl)-3,7-dihydro-3-methyl-1-[(4-methyl-2quinazolinyl)methyl].
The empirical formula is $C_{25}H_{28}N_8O_2$ and the molecular weight is 472.553 g/mol. The structural formula is:



PHARMACOLOGY:
Mechanism of action: Linagliptin Inhibits dipeptidyl peptidase-4, an enzyme that degrades the incretin hormones glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP). This results in increased concentrations of active incretin hormones, stimulating the release of insulin and decreasing levels of glucagon in the circulation.
Pharmacodynamics: Linagliptin binds to DPP-4 in a reversible manner and thus increases the concentrations of incretin hormones. Linagliptin glucose dependently increases insulin secretion and lowers glucagon secretion, thus resulting in better regulation of glucose homeostasis. Linagliptin binds selectively to DPP-4, and selectively inhibits DPP-4 but not DPP-8 or DPP-9 activity in vitro at concentrations approximating therapeutic exposures.
Pharmacokinetics:
Absorption: The absolute bioavailability of linagliptin is approximately 30%. High-fat meal reduced Cmax by 15% and increased AUC by 4%; this effect is not clinically relevant. Linagliptin may be administered with or without food.
Distribution: The mean apparent volume of distribution at steady state following a single intravenous dose of linagliptin 5 mg to healthy subjects is approximately 1110 L, indicating that linagliptin extensively distributes to the tissues. Plasma protein binding of linagliptin is concentration-dependent, decreasing from about 99% at 1 nmol/L to 75%-89% at ⩾ 30 nmol/L, reflecting saturation of binding to DPP-4 with increasing concentration of linagliptin. At high concentrations, where DPP-4 is fully saturated, 70% to 80% of linagliptin remains bound to plasma proteins and 20% to 30% is unbound in plasma. Plasma binding is not altered in patients with renal or hepatic impairment.
Metabolism: Following oral administration, the majority (about 90%) of linagliptin is excreted unchanged, indicating that metabolism represents a minor elimination pathway. A small fraction of absorbed linagliptin is metabolized to a pharmacologically inactive metabolite, which shows a steady-state exposure of 13.3% relative to linagliptin.
Excretion: Following administration of an oral [14C]-linagliptin dose to healthy subjects, approximately 85% of the administered radioactivity was eliminated via the enterohepatic system (80%) or urine (5%) within 4 days of dosing. Renal clearance at steady state was approximately 70 mL/min.

DOSAGE AND ADMINISTRATION:
Recommended dose is 5 mg orally once daily. Tablets may be taken with or without food.

Specific Populations:
Pregnancy: The limited data with Linagliptin use in pregnant women are not sufficient to inform of drug-associated risk for major birth defects and miscarriage. There are risks to the mother and fetus associated with poorly controlled diabetes in pregnancy.
Lactation: There is no information regarding the presence of linagliptin in human milk, the effects on the breastfed infant, or the effects on milk production.
Body mass index (BMI) / Weight: No dose adjustment is necessary based on BMI/weight. BMI/weight had no clinically meaningful effect on the pharmacokinetics of linagliptin based on a population pharmacokinetic analysis.
Gender: No dose adjustment is necessary based on gender. Gender had no clinically meaningful effect on the pharmacokinetics of linagliptin based on a population pharmacokinetic analysis.
Geriatric: Age did not have a clinically meaningful impact on the pharmacokinetics of linagliptin based on a population pharmacokinetic analysis.
Pediatric: Studies characterizing the pharmacokinetics of linagliptin in pediatric patients have not yet been performed.
Race: No dose adjustment is necessary based on race. Race had no clinically meaningful effect on the pharmacokinetics of Linagliptin based on available pharmacokinetic data, including subjects of White, Hispanic, Black, and Asian racial groups.
Renal impairment: No dose adjustment recommended.
Hepatic impairment: No dose adjustment recommended.
Pediatric use: Safety and efficacy of linagliptin in patients under 18 years of age have not been established.

INDICATIONS AND USAGE:
Linagliptin is indicated in adults as an adjunct to diet and exercise to improve glycemic control in adults with Type 2 Diabetes Mellitus.

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PRECAUTIONS:
Pancreatitis: There have been postmarketing reports of acute pancreatitis, including fatal pancreatitis, in patients taking Linagliptin. Take careful notice of potential signs and symptoms of pancreatitis. If pancreatitis is suspected, promptly discontinue linagliptiin and initiate appropriate management. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using Linagliptin.
Use with medications known to cause hypoglycemia: Insulin secretagogues and insulin are known to cause hypoglycemia. The use of linagliptin in combination with an insulin secretagogue (e.g., sulfonylurea) was associated with a higher rate of hypoglycemia compared with placebo in a clinical trial. The use of linagliptin in combination with insulin in subjects with severe renal impairment was associated with a higher rate of hypoglycemia. Therefore, a lower dose of the insulin secretagogue or insulin may be required to reduce the risk of hypoglycemia when used in combination with Linagliptin.
Pregnancy & lactation: Linagliptin has been assigned as category B drug by FDA. This drug should be used in pregnancy only if clearly indicated. It is not known whether linagliptin is excreted in human milk. Therefore caution should be exercised when this drug is administered to a nursing woman.

CONTRAINDICATIONS:
Linagliptin is contraindicated in patients with a history of a hypersensitivity reaction to linagliptin, such as urticaria, angioedema, or bronchial hyperreactivity. Linagliptin should not be used in patients with Type 1 Diabetes Mellitus or for the treatment of diabetic ketoacidosis, as it is not effective in these settings.
Insulin Secretagogues or Insulin: Co-administration of Linagliptin with an insulin secretagogue (e.g., sulfonylurea) or insulin may require lower doses of the insulin secretagogue or insulin to reduce the risk of hypoglycemia.

WARNINGS AND PRECAUTIONS:
Hypersensitivity reactions: Hypersensitivity reactions include anaphylaxis, angioedema, and exfoliative skin conditions. Onset of these reactions occurred predominantly within the first 3 months after initiation of treatment with Linagliptin, with some reports occurring after the first dose. If a serious hypersensitivity reaction is suspected, discontinue Linagliptin, assess for other potential causes for the event, and institute alternative treatment for diabetes.

DRUG INTERACTIONS:
Inducers of P-glycoprotein or CYP3A4 Enzymes: Rifampin decreased linagliptin exposure, suggesting that the efficacy of linagliptin may be reduced when administered in combination with a strong P-gp or CYP3A4 inducer. Therefore, use of alternative treatments is strongly recommended when linagliptin is to be administered with a strong P-gp or CYP3A4 inducer.

SIDE EFFECTS:
Metabolic: Metabolic side effects have included hypoglycemia, hyperlipidemia, hypertriglyceridemia and weight gain.
Hypersensitivity: Hypersensitivity side effects have included urticaria, angioedema, localized skin exfoliation, and bronchial hyperreactivity.
Respiratory: Respiratory side effects have included nasopharyngitis and cough. Side effects reported when linagliptin was used in combination with glimepiride and metformin include upper respiratory infection.
Musculoskeletal: Musculoskeletal side effects have included arthralgia, back pain and myalgia. Side effects reported when linagliptin was used in combination with glimepiride and metformin include pain in extremities.
Endocrine: Endocrine side effects have included pancreatitis.
Nervous system: Nervous system side effects have included headache.
Gastrointestinal: Gastrointestinal side effects reported include diarrhea. Side effects reported when linagliptin was added on to basal insulin therapy include constipation.
Genitourinary: Genitourinary side effects reported when linagliptin was used in combination with specific anti-diabetic agents include urinary tract infection.
Other: Increases in uric acid were reported more frequently in patients treated with linagliptin than placebo.

OVERDOSAGE:
In the event of an overdose, 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. Removal of linagliptin by hemodialysis or peritoneal dialysis is unlikely. 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.

INSTRUCTIONS:
- Store below 30ºC.
- Protect from heat, sunlight & moisture.
- Keep out of reach of children.
- To be sold on the prescription of a registered medical practitioner only.

PRESENTATION:

Lina Tablet 5 mg	:	Pack of 1 x 10 tablets.
Lina Tablet 5 mg	:	Pack of 2 x 7 tablets.
Lina Tablet 5 mg	:	Pack of 4 x 7 tablets.

ہدایات:
۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
گرمی، دھوپ اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔
صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔

FOR FURTHER INFORMATION PLEASE CONTACT:

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