SUMMARY PRODUCT CHARACTERISTICS

1. Name of the Medicinal Product

Linatin.

2. Qualitative and quantitative composition

Each film coated tablet contains:

Linagliptin 5.0mg.

For full list of excipients see section 6.1

3. Pharmaceutical Form

Tablets.

Light red, circular, biconvex film coated tablets, plain on both sides.

4. Clinical Particulars

4.1 Therapeutic Indications

Linagliptin is indicated in adult patients with type 2 diabetes mellitus (T2DM) to improve glycaemic control in conjunction with diet and exercise, as monotherapy or as add on to metformin, sulphonylureas, thiazolidinediones, insulin (with or without metformin and/or pioglitazone and/or sulphonylurea) or metformin plus sulphonylureas or metformin plus SGLT2 inhibitors.

4.2 Posology and method of administration Adults

The recommended dose is 5mg once daily. Linagliptin can be taken with or without a meal at any time of the day.

Renal impairment

No dose adjustment is required for patients with renal impairment.

Hepatic impairment

No dose adjustment is required for patients with hepatic impairment.

Elderly

No dose adjustment is necessary.

Children and adolescents

Linagliptin is not recommended for use in children below 18 years due to lack of data on safety and efficacy.

Missed dose

If a dose is missed, it should be taken as soon as the patient remembers. A double dose should not be taken at the same day.

4.3 Contraindications

Linatin® tablets is contraindicated in patients with known hypersensitivity to Linagliptin or to any excipients of the products.

4.4 Special warnings and precautions for use.

General:

Linagliptin should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.

Sulfonylureas are known to cause hypoglycemia. Patients receiving vildagliptin in combination with sulfonylurea may be at risk for hypoglycemia. Therefore, a lower dose of sulfonylurea may be considered to reduce the risk of hypoglycemia.

Pancreatitis

Acute pancreatitis has been observed in patients taking Linagliptin. If pancreatitis is suspected, Linagliptin should be discontinued.

Hypoglycaemia

Linagliptin alone showed a comparable incidence of hypoglycaemia to placebo. In clinical trials of Linagliptin as part of combination therapy with agents not known to cause hypoglycemia (metformin, thiazolidinediones) rates of hypoglycemia reported with Linagliptin were similar to rates in patients taking placebo.
Sulphonylureas are known to cause hypoglycaemia. Therefore, caution is advised when Linagliptin is used in combination with a sulphonylurea. A dose reduction of the sulphonylurea may be considered. Bullous Pemphigoid
Bullous pemphigoid has been observed in patients taking Linagliptin. If bullous pemphigoid is suspected, Linagliptin should be discontinued.

4.5 Interaction with other medicinal products and other forms of interaction.

Inducers of P-glycoprotein or CYPA4 Enzymes: Efficacy of Linatin® (Linagliptin) may be reduced when administered in combination with a strong P-gp or CYP 3A4 inducer. Therefore, use of alternative treatments is strongly recommended when Linagliptin is to be administered with P-gp or CYP 3A4 inducer.

4.6 Pregnancy and Lactation.

Pregnancy
There are no adequate data from the use of Linagliptin in pregnant women. Due to lack of human data, Linagliptin should not be used during pregnancy. Nursing Mothers
It is unknown whether Linagliptin is excreted in human milk. Animal studies have shown excretion of Linagliptin in milk. Linagliptin should not be used during breast-feeding.
Fertility
No studies on the effect on human fertility have been conducted for Linagliptin. No adverse effects on fertility were observed in animals upto the highest dose of 240mg/kg/day (approximately 943 times human exposure based on AUC comparisons).

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable effects.

The following adverse reactions have been reported during the use of Linagliptin:
Infections & infestations: Nasopharyngitis.
Immune system disorders: Hypersensitivity, Angioedema & urticaria.
Metabolism & Nutrition disorders: Hypoglycemia (when used in combination with metformin plus sulphonylurea, signs and symptoms of low blood sugar may include: headache, drowsiness, weakness, dizziness, confusion, irritability, hunger, fast heartbeat, sweating or feeling jittery), hypertriglyceridemia (when used in combination with sulphonylurea) & hyperlipidemia (when used in combination with pioglitazone).
Respiratory, thoracic & mediastinal disorders: Cough.
Gastrointestinal Disorders: Pancreatitis, constipation (when used in combination with insulin) & mouth ulceration.
Skin and subcutaneous tissue disorders: Rash & bullous pemphigoid.
Reporting of suspected adverse reactions:
Reporting suspected adverse reactions after authorisation of the medicinal product is important.It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to the marketing authorisation holder, or, if available, via the national reporting system.

4.9 Overdose.

In the event of an overdose, supportive management is recommended. Linagliptin is not expected to be eliminated to a therapeutically significant degree by hemodialysis or peritoneal dialysis.

5. Pharmacological Properties.

5.1 Pharmacodynamic Properties.

Pharmacotherapeutic group: Drugs used in diabetes, dipeptidyl peptidase 4 (DPP-4) inhibitors. **ATC code:** A10BH05.

Mechanism of action

Linagliptin is an inhibitor of 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 meals 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 of hepatic glucose output.

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 a better regulation of the 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.

5.2 Pharmacokinetic Properties.

Absorption

The absolute bioavailability of linagliptin is approximately 30%. Co-administration of a high-fat meal with linagliptin has no clinically relevant effect on the pharmacokinetics, linagliptin may be administered with or without food.

Distribution

As a result of tissue binding, the mean apparent volume of distribution at steady state following a single 5mg intravenous dose of Linagliptin to healthy subjects is approximately 1110 litres, indicating that Linagliptin extensively distributes to the tissues. Plasma protein binding of Linagliptin is concentration dependant, 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.

Metabolism

An oral dose of Linagliptin is excreted primarily in the feaces. 90% of an oral dose is excreted unchanged in the urine and feaces. The predominant metabolite in the plasma is CD1790 and the predominant metabolite recovered after excretion is M489(1). Other metabolites are produced through oxidation, oxidative degradation, n-acetylation, glucuronidation, and cysteine adduct formation2. Other metabolites have been identified through mass spectrometry though no structures are determined. Metabolism of linagliptin is mediated by cytochrome P450 3A4, aldo-keto reductases, and carbonyl reductases.

Elimination

About 84.7% of Linagliptin is eliminated in the feaces and 5.4% is eliminated in the urine. The terminal half-life of Linagliptin is 155 hours. Renal clearance at steady state is approximately 70mL/min.

5.3 Preclinical safety data

Liver, kidneys and gastrointestinal tract are the principal target organs of toxicity in mice and rats at repeat doses of linagliptin of more than 300 times the human exposure.

In rat's effects on reproductive organs, thyroid and the lymphoid organs were seen at more than 1,500 times human exposure. Strong pseudo-allergic reactions were observed in dogs at medium doses, secondarily causing cardiovascular changes, which were considered dog-specific. Liver, kidneys, stomach, reproductive organs, thymus, spleen, and lymph nodes were target organs of toxicity in Cynomolgus monkeys at more than 450 times human exposure. At more than 100 times human exposure, irritation of the stomach was the major finding in these monkeys.
Linagliptin and its main metabolite did not show any genotoxic potential.

6. Pharmaceutical Particulars.

6.1 List of excipients.

Mannitol
Pregelatinized Starch
Maize Starch
Povidone K-30
Crospovidone
Magnesium Stearate
Hypromellose
Titanium Dioxide
Polyethylene Glycol 6000
Purified Talc
Red Iron Oxide
Yellow Iron Oxide
Isopropyl Alcohol
Methylene Chloride.

6.2 Incompatibilities:

None known.

6.3 Shelf life:

24 months.

6.4 Special Precautions for storage:

Store in a dry place below 30°C
Protect from light and moisture.
Keep all medicines out of reach of children.

6.5 Nature and contents of the container:

Packed in blisters of 1x10's, 2x14's, 4x14's, 2x10's, 3x10's, 6x10's and 10x10's and contained in a unit box along with literature insert.

6.6 Special precautions for disposal:

Any unused product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorization Holder and Manufacturing facility:

Company Name: Laboratory & Allied Ltd.
Address: Plot No.: 209/10349 Opposite Sameer Business Park Next To Libra House Mombasa Road, P.O Box 42875, Code 00100 Nairobi, Kenya.
Telephone: + 254 – 20-8040306. Telefax: 254 – 020 – 8040309. E-Mail: Info@Laballied.Com

Manufacturer

Company Name: Laboratory & Allied Ltd.
Address: Plot No: 209/10349 Opposite Sameer Business Park Next to Libra House Mombasa Road, P.O Box 42875, Code 00100 Nairobi, Kenya.
Telephone: + 254 – 20-8040306.

Telefax: 254 – 020 – 8040309.
E-Mail: info@laballied.com

8. Marketing authorization Number

H2025/CTD10726/22727

9. Date of First Registration/Renewal

20/01/2025

10. Date of Revision of text

20/01/2025