1. NAME OF THE MEDICINAL PRODUCTS

Lenglar® (Insulin Glargine Injection 100 IU/mL), Solution for Injection in 3 mL Multi-dose Cartridge (MDC) pack presentation.

Lenglar® (Insulin Glargine Injection) is a biosimilar product of Lantus®.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL contains:
Insulin Glargine Ph. Eur. …..100 IU
m-Cresol USP …..0.27% w/v (as preservative)
Water for Injection USP …. q.s.

Each 1 mL contains 100 IU Insulin Glargine (produced in non-pathogenic strain *Escherichia coli* by recombinant DNA technology)

Each 3 mL Cartridge of Insulin Glargine Injection 100 IU/mL solution of injection is equivalent to 300 international units.

For full list of excipients, please refer section 6.1: List of excipients.

Insulin Glargine Injection is a sterile clear and colourless solution of Insulin Glargine for subcutaneous use.

3. PHARMACEUTICAL FORM

Solution for Injection

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Treatment of diabetes mellitus in adults, adolescents and children aged 2 years and above.

4.2 Posology and Method of Administration

Posology

Lenglar® contains insulin glargine, an insulin analogue, and has a prolonged duration of action. Insulin glargine should be administered once daily at any time but at the same time each day.

The dose regimen (dose and timing) should be individually adjusted. In patients with type 2 diabetes mellitus, insulin glargine can also be given together with orally active antidiabetic medicinal products. The potency of this medicinal product is stated in units. These units are exclusive to insulin glargine and are not the same as IU or the units used to express the potency of other insulin analogues.

Special population

Elderly population (≥65 years old)

In the elderly, progressive deterioration of renal function may lead to a steady decrease in insulin requirements.

Renal impairment

In patients with renal impairment, insulin requirements may be diminished due to reduced insulin metabolism.

Hepatic impairment

In patients with hepatic impairment, insulin requirements may be diminished due to reduced capacity for gluconeogenesis and reduced insulin metabolism.

Pediatric population

- Adolescents and children aged 2 years and older patients

  Safety and efficacy of insulin glargine have been established in adolescents and children aged 2 years and older. The dose regimen (dose and timing) should be individually adjusted.

- Children below 2 years of age

The safety and efficacy of insulin glargine have not been established. No data are available.

Switch from other insulins to insulin glargine

When switching from a treatment regimen with an intermediate or long-acting insulin to a regimen with insulin glargine, a change of the dose of the basal insulin may be required and the concomitant antidiabetic treatment may need to be adjusted (dose and timing of additional regular insulins or fast-acting insulin analogues or the dose of oral antidiabetic medicinal products).

Switch from twice daily NPH insulin to insulin glargine

To reduce the risk of nocturnal and early morning hypoglycaemia, patients who are changing their basal insulin regimen from a twice daily NPH insulin to a once daily regimen with insulin glargine Insulin glargine should reduce their daily dose of basal insulin by 20-30% during the first weeks of treatment.

Switch from insulin glargine 300 units/ml to insulin glargine 100 units/ml

Insulin glargine 100 units/ml and Toujeo (insulin glargine 300 units/ml) are not bioequivalent and are not directly interchangeable. To reduce the risk of hypoglycemia, patients who are changing their basal insulin regimen from an insulin regimen with once daily insulin glargine 300 units/ml to a once daily regimen with Insulin glargine 100 units/ml should reduce their dose by approximately 20%.

During the first weeks the reduction should, at least partially, be compensated by an increase in mealtime insulin, after this period the regimen should be adjusted individually.

Close metabolic monitoring is recommended during the switch and in the initial weeks thereafter. With improved metabolic control and resulting increase in insulin sensitivity a further adjustment

in dose regimen may become necessary. Dose adjustment may also be required, for example, if the patient's weight or life-style changes, change of timing of insulin dose or other circumstances arise that increase susceptibility to hypo-or hyperglycaemia (see section 4.4).

Patients with high insulin doses because of antibodies to human insulin may experience an improved insulin response with Insulin glargine 100 units/ml

Method of administration

Insulin glargine is administered subcutaneously.

Insulin glargine should not be administered intravenously. The prolonged duration of action of insulin glargine is dependent on its injection into subcutaneous tissue. Intravenous administration of the usual subcutaneous dose could result in severe hypoglycaemia.

There are no clinically relevant differences in serum insulin or glucose levels after abdominal, deltoid or thigh administration of insulin glargine. Injection sites must be rotated within a given injection area from one injection to the next in order to reduce the risk of lipodystrophy and cutaneous amyloidosis (see section 4.4 and 4.8).

insulin glargine must not be mixed with any other insulin or diluted. Mixing or diluting can change its time/action profile and mixing can cause precipitation.

4.3 Contraindications

Insulin glargine is contraindicated

- During episodes of hypoglycemia
- In patients with hypersensitivity to Insulin glargine or one of its excipients

4.4 Special Warnings and Precautions for Use

Never Share A Insulin glargine Cartridge or Needle Between Patients

Insulin glargine cartridges must never be shared between patients, even if the needle is changed. Patients using Insulin glargine must never reuse or share needles with another person. Sharing poses a risk for transmission of blood-borne pathogens.

Hyperglycemia or Hypoglycemia with changes in Insulin Regimen

Changes in insulin strength, manufacturer, type, or method of administration may affect glycemic control and predispose to hypoglycemia or hyperglycemia. These changes should be made cautiously and only under close medical supervision, and the frequency of blood glucose monitoring should be increased. For patients with type 2 diabetes, dosage adjustments of concomitant oral and anti-diabetic products may be needed.

Hypoglycemia

Hypoglycemia is the most common adverse reaction associated with insulin, including Insulin glargine. Severe hypoglycemia can cause seizures, may be life-threatening or cause death. Hypoglycemia can impair concentration ability and reaction time; this may place an individual and others at risk in situations where these abilities are important (e.g., driving or operating other machinery).

Hypoglycemia can happen suddenly and symptoms may differ in each individual and change over time in the same individual. Symptomatic awareness of hypoglycemia may be less pronounced in patients with longstanding diabetes, in patients with diabetic nerve disease, in patients using medications that block the sympathetic nervous system (e.g., beta-blockers), or in patients who experience recurrent hypoglycemia.

Risk Factors For Hypoglycemia

The risk of hypoglycemia after an injection is related to the duration of action of the insulin and, in general, is highest when the glucose lowering effect of the insulin is maximal. As with all insulin preparations, the glucose lowering effect time course of Insulin glargine may vary in different individuals or at different times in the same individual and depends on many conditions, including the area of injection as well as the injection site blood supply and temperature. Other factors which may increase the risk of hypoglycemia include changes in meal pattern (e.g., macronutrient content or timing of meals), changes in level of physical activity, or changes to co-administered medication. Patients with renal or hepatic impairment may be at higher risk of hypoglycemia.

Risk Mitigation Strategies For Hypoglycemia

Patients and caregivers must be educated to recognize and manage hypoglycemia. Self-monitoring of blood glucose plays an essential role in the prevention and management of hypoglycemia. In patients at higher risk for hypoglycemia and patients who have reduced symptomatic awareness of hypoglycemia, increased frequency of blood glucose monitoring is recommended. The long-acting effect of Insulin glargine may delay recovery from hypoglycemia.

Medication Errors

Accidental mix-ups among insulin products, particularly between long-acting insulins and rapid-acting insulins, have been reported. To avoid medication errors between Insulin glargine and other insulin's, instruct patients to always check the insulin label before each injection.

Hypersensitivity and Allergic Reactions

Severe, life-threatening, generalized allergy, including anaphylaxis, can occur with insulin products, including Insulin Glargine. If hypersensitivity reactions occur, discontinue Insulin Glargine; treat per standard of care and monitor until symptoms and signs resolve. Insulin Glargine is contraindicated in patients who have had hypersensitivity reactions to Insulin Glargine or one of the excipients.

Hypokalemia

All insulin products, including Insulin glargine, cause a shift in potassium from the extracellular to intracellular space, possibly leading to hypokalemia. Untreated hypokalemia may cause respiratory paralysis, ventricular arrhythmia, and death. Monitor potassium levels in patients at risk for hypokalemia if indicated (e.g., patients using potassium-lowering medications, patients taking medications sensitive to serum potassium concentrations).

Fluid Retention and Heart Failure With Concomitant Use Of PPAR-gamma Agonists

Thiazolidinediones (TZDs), which are peroxisome proliferator-activated receptor (PPAR)-gamma agonists, can cause dose-related fluid retention, particularly when used in combination with

insulin. Fluid retention may lead to or exacerbate heart failure. Patients treated with insulin, including Insulin glargine, and a PPAR-gamma agonist should be observed for signs and symptoms of heart failure. If heart failure develops, it should be managed according to current standards of care, and discontinuation or dose reduction of the PPAR-gamma agonist must be considered.

4.5 Interactions with Other Medicinal Products and Other Forms of Interaction

A number of substances affect glucose metabolism and may require Insulin dose adjustment. Substances that may enhance the blood glucose lowering effect and susceptibility to hypoglycaemia include: oral antidiabetic agents, ACE inhibitors, pentoxifylline, perhexiline, disopyramide, fibrates, fluoxetine, MAO inhibitors, dextropropoxyphene, salicylates, sulfonamide antibiotics.
Substances that may reduce the blood glucose lowering effect and susceptibility to hyperglycaemia include: corticosteroids, danazol, diazoxide, diuretics, glucagon, isoniazid, oral contraceptives, phenothiazine derivatives, somatotrophin, sympathomimetic agents (e.g. epinephrine [adrenaline], salbutamol, terbutaline), thyroid hormones, protease inhibitors and atypical antipsychotic medications (e.g. olanzapine and clozapine).
Beta-blockers, clonidine, lithium salts or alcohol may either potentiate or weaken the blood glucose lowering effect of Insulin. Pentamidine may cause hypoglycaemia, which may be sometimes be followed by hyperglycaemia.
In addition, under the influence of sympatholytic medicinal products such as beta-blockers, clonidine, guanethidine and reserpine, the signs of adrenergic counter-regulation may be reduced or absent.

4.6 Fertility, Pregnancy and Lactation

Pregnancy
For Insulin Glargine no clinical data on exposed pregnancies from controlled clinical studies are available. A large amount of data on pregnant women (more than 1000 pregnancy outcomes) indicate no specific adverse effects of Insulin Glargine on pregnancy and no specific malformative nor feto/neonatal toxicity of Insulin Glargine. Animal data do not indicate reproductive toxicity.
The use of Insulin glargine may be considered during pregnancy, if clinically needed.
It is essential for patients with pre-existing or gestational diabetes to maintain good metabolic control throughout pregnancy to prevent adverse outcomes associated with hyperglycemia. Insulin requirements may decrease during the first trimester and generally increase during the second and third trimesters. Immediately after delivery, insulin requirements decline rapidly (increased risk of hypoglycaemia). Careful monitoring of glucose control is essential.

Breast-feeding
It is unknown whether Insulin Glargine is excreted in human milk. No metabolic effects of ingested Insulin Glargine on the breast-fed newborn/infant are anticipated since Insulin Glargine as a peptide is digested into aminoacids in the human gastrointestinal tract. Breast-feeding women may require adjustments in insulin dose and diet.

Fertility

Reported animal studies on Insulin Glargine do not indicate direct harmful effects with respect to fertility.

4.7 Effects on Ability to Drive and Use Machines

The patient's ability to concentrate and react may be impaired as a result of hypoglycaemia. This may constitute a risk in situations where these abilities are of special importance (e.g. driving a car or operating machinery).

Patients should be advised to take precautions to avoid hypoglycaemia whilst driving, this is particularly important in those who have reduced or absent awareness of the warning signs of hypoglycaemia or have frequent episodes of hypoglycaemia. The advisability of driving should be considered in these circumstances.

4.8 Undesirable Effects

Summary of the safety profile

Hypoglycaemia (very common), in general the most frequent adverse reaction of insulin therapy, may occur if the insulin dose is too high in relation to the insulin requirement (see section 4.4).

Tabulated list of adverse reactions

The following related adverse reactions from reported clinical investigations are listed below by system organ class and in order of decreasing incidence (very common: ≥1/10; common: ≥1/100 to <1/10; uncommon: ≥1/1,000 to <1/100; rare: ≥1/10,000 to <1/1,000; very rare: <1/10,000). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

MedDRA system organ classes	**Very common**	**Common**	**Uncommon**	**Rare**	**Very rare**	**Not Known**
Immune system disorders				Allergic reactions		
Metabolism and nutrition disorders	Hypoglycaemia					
Nervous system disorders					Dysgeusia	
Eyes disorders				Visual impairment Retinopathy		
Skin and subcutaneous tissue disorders		Lipohypertrophy	Lipoatrophy			Cutaneous amyloidosis
Musculoskeletal and connective tissue disorders					Myalgia	
General disorders and administration site conditions		Injection site reactions		Oedema		

Description of selected adverse reactions

Metabolism and nutrition disorders

Severe hypoglycaemic attacks, especially if recurrent, may lead to neurological damage. Prolonged or severe hypoglycaemic episodes may be life-threatening.

In many patients, the signs and symptoms of neuroglycopenia are preceded by signs of adrenergic counter-regulation. Generally, the greater and more rapid the decline in blood glucose, the more marked is the phenomenon of counter-regulation and its symptoms (see section 4.4).

Immune system disorders

Immediate-type allergic reactions to insulin are rare. Such reactions to insulin (including insulin glargine) or the excipients may, for example, be associated with generalised skin reactions, angio-oedema, bronchospasm, hypotension and shock, and may be life-threatening.

Eyes disorders

A marked change in glycaemic control may cause temporary visual impairment, due to temporary alteration in the turgidity and refractive index of the lens.

Long-term improved glycaemic control decreases the risk of progression of diabetic retinopathy. However, intensification of insulin therapy with abrupt improvement in glycaemic control may be associated with temporary worsening of diabetic retinopathy. In patients with proliferative retinopathy, particularly if not treated with photocoagulation, severe hypoglycaemic episodes may result in transient amaurosis.

Skin and subcutaneous tissue disorders

Lipodystrophy may occur at the injection site and delay local insulin absorption. Continuous rotation of the injection site within the given injection area may help to reduce or prevent these reactions.

General disorders and administration site conditions

Injection site reactions include redness, pain, itching, hives, swelling, or inflammation. Most minor reactions to insulins at the injection site usually resolve in a few days to a few weeks.

Rarely, insulin may cause sodium retention and oedema particularly if previously poor metabolic control is improved by intensified insulin therapy.

Paediatric population

In general, the safety profile for children and adolescents (≤18 years of age) is similar to the safety profile for adults.

The adverse reaction mentioned in reported post marketing surveillance included relatively more frequent injection site reactions (injection site pain, injection site reaction) and skin reactions (rash, urticaria) in children and adolescents (≤18 years of age) than in adults.

Clinical study safety data are not available for children under 2 years.

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.

4.9 Overdose

Excess insulin administration may cause hypoglycemia and hypokalemia. Mild episodes of hypoglycemia can usually be treated with oral carbohydrates. Adjustments in drug dosage, meal patterns, or exercise may be needed.

More severe episodes of hypoglycemia with coma, seizure, or neurologic impairment may be treated with intramuscular/subcutaneous glucagon or concentrated intravenous glucose. After apparent clinical recovery from hypoglycemia, continued observation and additional carbohydrate intake may be necessary to avoid recurrence of hypoglycemia. Hypokalemia must be corrected appropriately.

It is therefore recommended that the diabetic patient constantly carry some sugar lumps, sweets, biscuits, or sugary fruit juice. Adjustments in drug dosage, meal patterns, or exercise, may be needed.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Drugs used in diabetes, insulins and analogues for injection, long-acting

ATC (Anatomical Therapeutic Chemical) Classification Code: A10AE04

Insulin glargine is a long acting insulin preparation.

5.1 Pharmacodynamic Properties:

Mechanism of action

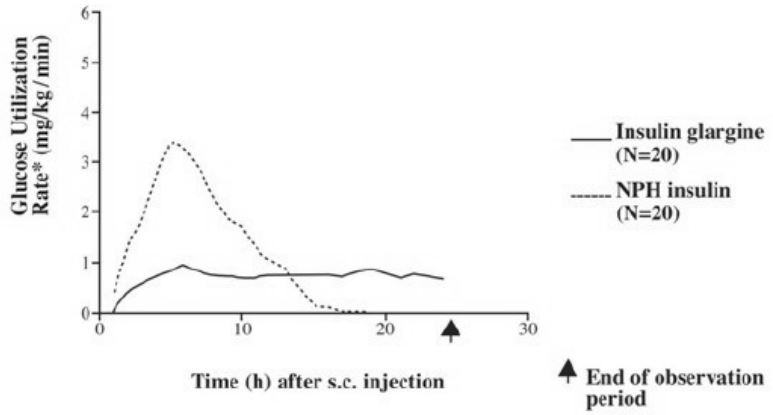
Insulin Glargine is a human insulin analogue designed to have a low solubility at neutral pH. It is completely soluble at the acidic pH of the Insulin glargine injection solution (pH 4). After injection into the subcutaneous tissue, the acidic solution is neutralised leading to formation of micro-precipitates from which small amounts of Insulin Glargine are continuously released, providing a smooth, peakless, predictable concentration/time profile with a prolonged duration of action.

Insulin Glargine is metabolised into 2 active metabolites M1 and M2 (see section 5.2).

Insulin receptor binding: *In vitro* studies indicate that the affinity of Insulin Glargine and its metabolites M1 and M2 for the human insulin receptor is similar to the one of human insulin.
IGF-1 receptor binding: The affinity of Insulin Glargine for the human IGF-1 receptor is approximately 5 to 8-fold greater than that of human insulin (but approximately 70 to 80-fold lower than the one of IGF-1), whereas M1 and M2 bind the IGF-1 receptor with slightly lower affinity compared to human insulin.
The total therapeutic insulin concentration (Insulin Glargine and its metabolites) found in type 1 diabetic patients was markedly lower than what would be required for a half maximal occupation of the IGF-1 receptor and the subsequent activation of the mitogenic-proliferative pathway initiated by the IGF-1 receptor. Physiological concentrations of endogenous IGF-1 may activate the mitogenic-proliferative pathway; however, the therapeutic concentrations found in insulin therapy, including in Insulin Glargine therapy, are considerably lower than the pharmacological concentrations required to activate the IGF-1 pathway.
The primary activity of insulin, including Insulin Glargine, is regulation of glucose metabolism. Insulin and its analogues lower blood glucose levels by stimulating peripheral glucose uptake, especially by skeletal muscle and fat, and by inhibiting hepatic glucose production. Insulin inhibits lipolysis in the adipocyte, inhibits proteolysis and enhances protein synthesis.

In clinical studies, the glucose-lowering effect on a molar basis (i.e., when given at the same doses) of intravenous Insulin Glargine is approximately the same as human insulin. In euglycemic clamp studies in healthy subjects or in patients with type 1 diabetes, the onset of action of subcutaneous Insulin Glargine was slower than NPH human insulin. The effect profile of Insulin Glargine was relatively constant with no pronounced peak and the duration of its effect was prolonged compared to NPH human insulin. ***Figure 1*** shows results from a study in patients with type 1 diabetes conducted for a maximum of 24 hours after the injection. The median time between injection and the end of pharmacological effect was 14.5 hours (range: 9.5 to 19.3 hours) for NPH human insulin, and 24 hours (range: 10.8 to > 24.0 hours) (24 hours was the end of the observation period) for Insulin Glargine.

Figure 1: Activity Profile in Patients with Type 1 Diabetes†



* Determined as amount of glucose infused to maintain constant plasma glucose levels (hourly mean values); indicative of insulin activity.
† Between-patient variability (CV, coefficient of variation); insulin glargine, 84% and NPH, 78%.

The longer duration of action of subcutaneous Insulin Glargine is directly related to its slower rate of absorption and supports once daily administration. The time course of action of insulin and insulin analogues such as Insulin Glargine may vary considerably in different individuals or within the same individual.

A study to compare Pharmacokinetics and Pharmacodynamics of Wockhardt's Insulin Glargine with Lantus® in Healthy Subjects was conducted.

The objective of the study was to obtain estimates of mean and variability of pharmacokinetic parameters (C_{max} and AUC_{0-24h}) and pharmacodynamic parameters ($AUC_{GIR\ 0-24h}$ and GIR_{max}) and to demonstrate average bioequivalence in the pharmacokinetic (PK) endpoints of Wockhardt's long acting human recombinant insulin analogue Glargine (Wockhardt insulin glargine and Lantus® as well as assessing safety and local tolerability of the two insulin preparations in Healthy subjects.

Overall, of the 40 subjects enrolled in the study all of them were Asian (100%) and male (100%). The mean age for all subjects was 31.1 years (range 19 to 44 years), the mean height was 167.6 cm (range 156.0 to 183.5 cm), the mean weight was 62.08 kg (range 50.9 to 84.3 kg) and mean BMI was 22.1 (range 18.69 to 26.91). Mean fasting blood glucose levels were 72.56 mg/dL (range 63 to 89 mg/dL).

Summary statistics and bioequivalence analysis of the PK and PD of the two insulin glargine formulations are shown in the table below. Analysis of the primary PK endpoints showed that the CI 90% of the geometric LS mean ratio for C_{max} and AUC_{0-24h} was entirely contained within the bioequivalence interval of 80% to 125%.

The results for the PD endpoints also support the bioequivalence for Wockhardt's Insulin Glargine

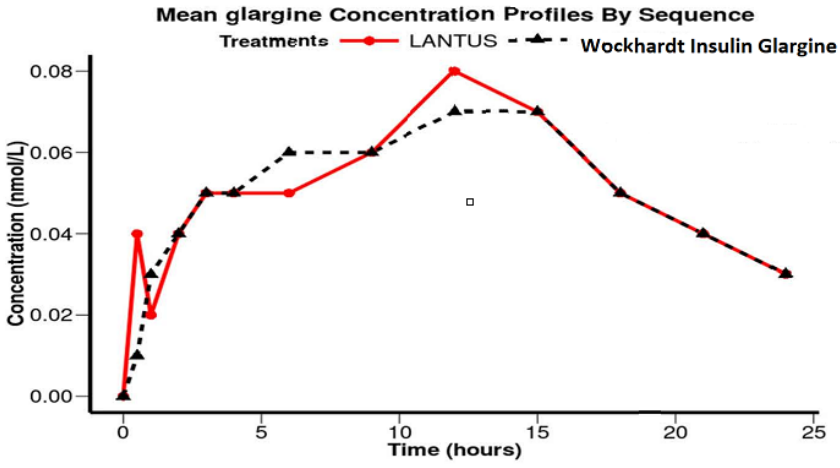
and Lantus®, as the CI95% of the geometric LS mean ratios for $AUC_{GIR\ 0\text{-}24h}$ and GIR_{max} were entirely contained within the bioequivalence interval of 80% to 125%.

Bioequivalence Analysis of Pharmacokinetic & Pharmacodynamic Parameters

	Geometric Least Square Mean					Between Subject Variability (%)		Within Subject Variability (%)	
Primary Pk Parameters	**Wockhardt's Insulin Glargine N=69**	**Lantus N=65**	**Ratio**	**90% CI Of The Ratio**		**Lantus**	**Wockhardt's Insulin Glargine**	**Lantus**	**Wockhardt's Insulin Glargine**
$AUC_{0\text{-}24}$ (h*nmol/L)	1.09	1.05	1.04	0.91	1.18	53	50	46	38
Cmax (nmol/L)	0.08	0.08	0.96	0.86	1.08	31	31	48	25
Primary PD Parameters	**Wockhardt's Insulin Glargine N=71**	**Lantus N=73**	**Ratio**	**95% CI Of The Ratio**		**Lantus**	**Wockhardt's Insulin Glargine**	**Lantus**	**Wockhardt's Insulin Glargine**
$AUC_{GIR0\text{-}24}$ (h*mg/kg/min)	20.99	21.63	0.97	0.80	1.17	58	68	57	56
GIR_{MAX}	1.82	1.85	0.98	0.85	1.14	40	48	42	44

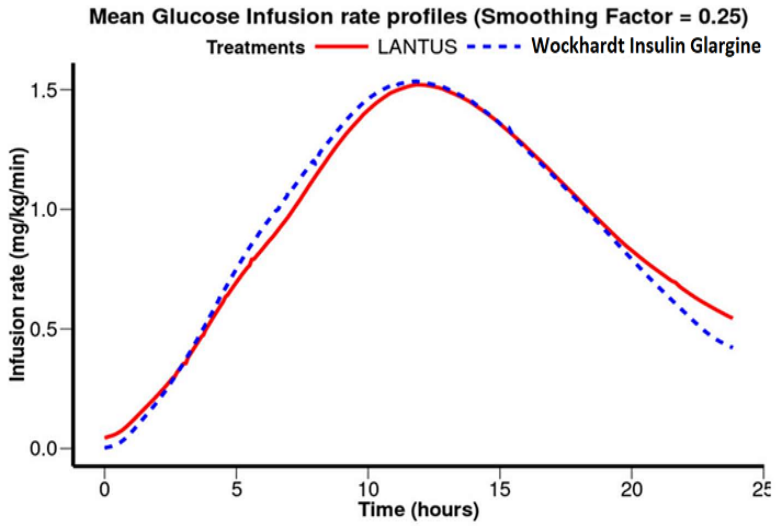
A plot of mean plasma glargine concentrations versus time since dose for Wockhardt insulin glargine and **Lantus®** is shown in ***Figure 2*** below. Visual inspection of the figure reveals comparable concentration versus time profiles for Wockhardt insulin glargine and **Lantus®**.

Figure 2: Mean Plasma Glargine Concentration vs. Time by Formulation



Glucose Infusion Rate (GIR): A plot of mean smoothed GIR versus time since dose for Wockhardt insulin glargine and Lantus® is shown in ***Figure 3*** below. Visual inspection of the figure reveals comparable GIR versus time profiles for Wockhardt insulin glargine and Lantus®.

Figure 3: Mean glucose infusion rate vs. Time by Formulation



Safety Results:

In this study, a total of 8 AEs were observed in 6 subjects, of them 2 subjects had received the treatment injection Wockhardt insulin glargine and 4 subjects had received reference treatment injection Lantus®.

All AEs in this study recovered without sequel.

Local tolerability assessments at the injection site reaction did not show any significant observations of erythema, induration, itching and oedema at 24 hours, pain on palpation and spontaneous pain post at 12 hours and 24 hours of the Wockhardt insulin glargine and Lantus® injection.

There were no clinically significant observations noted in laboratory examinations which included hematology, biochemistry, urinalysis, blood glucose and total cholesterol. The analysis of AEs, clinical laboratory evaluation and vital signs examination demonstrated that Wockhardt insulin glargine is well tolerated and has a favorable safety profile.

Conclusion:

Wockhardt insulin glargine and Lantus® are bioequivalent based on the results for the primary PK and PD endpoints. The CI90% for the geometric LS mean ratio was entirely contained within the bioequivalence interval of 80% to 125% for $AUC_{0\text{-}24h}$, and C_{max} the primary PK end points. These results indicate similar rate and extent of absorption for the two formulations. The CI 95% of the geometric LS mean ratios for primary PD end points - $AUC_{GIR\ 0\text{-}24h}$ and GIR_{max} were also entirely

contained within the bioequivalence interval of 80% to 125%. Based on analysis of AEs, clinical laboratory evaluation, local tolerability test and vital signs examination it is demonstrated that Wockhardt insulin glargine is well tolerated and has a comparable safety profile to Lantus®.
In conclusion, this study demonstrated the PK and PD bioequivalence of Wockhardt insulin glargine and Lantus® and both the formulations were comparably safe and well tolerated after administration of 0.4 U/kg dose.

5.2 Pharmacokinetic Properties

In healthy subjects and diabetic patients, insulin serum concentrations indicated a slower and much more prolonged absorption and showed a lack of a peak after subcutaneous injection of insulin glargine in comparison to human NPH insulin. Concentrations were thus consistent with the time profile of the pharmacodynamic activity of insulin glargine. The graph above shows the activity profiles over time of insulin glargine and NPH insulin.

Insulin glargine injected once daily will reach steady state levels in 2-4 days after the first dose.

When given intravenously the elimination half-life of insulin glargine and human insulin were comparable.

After subcutaneous injection of Insulin glargine in diabetic patients, insulin glargine is rapidly metabolized at the carboxyl terminus of the Beta chain with formation of two active metabolites M1 (21A-Gly-insulin) and M2 (21A-Gly-des-30B-Thr-insulin). In plasma, the principal circulating compound is the metabolite M1. The exposure to M1 increases with the administered dose of Insulin glargine. The pharmacokinetic and pharmacodynamic findings indicate that the effect of the subcutaneous injection with Insulin glargine is principally based on exposure to M1. Insulin glargine and the metabolite M2 were not detectable in the vast majority of subjects and, when they were detectable their concentration was independent of the administered dose of Insulin glargine.
In clinical studies, subgroup analyses based on age and gender did not indicate any difference in safety and efficacy in insulin glargine-treated patients compared to the entire study population.

Pediatric population
Pharmacokinetics in children aged 2 to less than 6 years with type 1 diabetes mellitus was assessed in one clinical study. Plasma “trough” levels of insulin glargine and its main M1 and M2 metabolites were measured in children treated with insulin glargine, revealing plasma

concentration patterns similar to adults, and providing no evidence for accumulation of insulin glargine or its metabolites with chronic dosing.

5.3 Preclinical Safety Data

Non-clinical data on Insulin Glargine reveal no special hazard for humans based on reported conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Zinc Chloride, m-Cresol, Glycerol (85%), Sodium Hydroxide (for pH adjustment), Hydrochloric acid (for pH adjustment) and Water for Injection (WFI).

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products.

6.3 Shelf Life

Unopened cartridges- 36 months

After first use- 28 days

6.4 Special Precautions for Storage

Lenglar® Cartridge which is not in use should be stored in a refrigerator (+2° to +8° C) but not allowed to freeze.

Once opened, Lenglar® Cartridge should be stored at temperature not above 30 °C for up to 4 weeks.

Do not expose to heat and direct sunlight. Lenglar® Cartridge must be kept out of reach of children.

Insulin Glargine must only be used if the solution is clear and colourless with no particles visible.

Insulin Glargine must not be mixed with any other Insulin nor be diluted. Mixing or diluting can change its time/action profile and mixing can cause precipitation.

Unopened cartridges

Store in a refrigerator (2°C - 8°C).

After first use

Store below 30°C

6.5 Nature and Contents of Container

1 x 3 mL:

3 mL clear tubular Type 1 glass cartridge with aluminium top seal with Bromobutyl rubber disc and Bromobutyl red bottom plunger. One cartridge is packed into an outer carton.

5 x 3 mL:

3 mL clear tubular Type 1 glass cartridge with aluminium top seal with Bromobutyl rubber disc and Bromobutyl red bottom plunger. Five cartridges are packed into an outer carton.

6.6 Special Precautions for Disposal and Other Handling

Inspect Lenglar® before use. It must only be used if the solution is clear, colourless, with no solid particles visible, and if it is of water-like consistency. Since Lenglar® is a solution, it does not require re-suspension before use.

Lenglar® must not be mixed with any other insulin or diluted. Mixing or diluting can change its time/action profile and mixing can cause precipitation.

Insulin label must always be checked before each injection to avoid medication errors between Insulin Glargine and other Insulins.

Lenglar® 3 mL cartridge can be used with Wockhardt's mypen®2 (Reusable Insulin Delivery Device)

7. MANUFACTURER

Wockhardt Limited

E-1/1, Wockhardt Infrastructure Development Limited,

Special Economic Zone (SEZ), E-1, Shendra MIDC Five Star Industrial Area, Shendra,

Chhatrapati Sambhajinagar (Aurangabad)-431154, Maharashtra State,

India

8. PRODUCT REGISTRATION HOLDER

NVS REGULATORY SERVICES SDN BHD.
19G, 7TH FLOOR, BLOCK 2,
WORLDWIDE BUSINESS CENTRE,
JALAN TINJU 13/50
40675 SHAH ALAM
MALAYSIA

9. DATE OF REVISION

March 2026