

LANTUS**1. NAME OF THE MEDICINAL PRODUCT**

Lantus 100 Units/ml solution for injection in a cartridge, cartridge for OptiClik, pre-filled pen (Optiset or Solostar) or in a vial.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains 100 Units insulin glargine (equivalent to 3.64 mg).

Each vial contains 10 ml of solution for injection, equivalent to 1000 Units

Each cartridge contains 3 ml of solution for injection, equivalent to 300 Units

Each pre-filled pen contains 3 ml of solution for injection, equivalent to 300 Units

Insulin glargine is produced by recombinant DNA technology in *Escherichia coli*.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection

Clear colourless solution.

4. CLINICAL PARTICULARS**4.1 Therapeutic indications**

Treatment of adult and pediatric patients 6 years and over with type 1 diabetes mellitus or adults patients with type 2 diabetes mellitus who require basal (long acting) insulin for the control of hyperglycemia .

4.2 Posology and method of administration

~~The potency of this preparation is stated in units. These units are exclusive to Lantus and are not the same as IU or the units used to express the potency of other insulin analogues. See section 5.1 (Pharmacodynamics).~~

~~Lantus contains insulin glargine, an insulin analogue with a prolonged duration of action. It should be administered once daily at any time but at the same time each day.~~

~~The dosage and timing of dose of Lantus should be individually adjusted. In patients with type 2 diabetes mellitus, Lantus can also be given together with orally active antidiabetic medicinal products.~~

Children

~~In children efficacy and safety of Lantus have only been demonstrated when given in the evening.~~

~~Due to limited experience the efficacy and safety of Lantus have not been demonstrated in children below the age of 6 years.~~

Posology

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

The Lantus dose regimen (dose and timing) should be individually adjusted. In patients with type 2 diabetes mellitus, Lantus 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 Lantus and are not the same as IU or the units used to express the potency of other insulin analogues. (see section 5.1).

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.

Paediatric population

Safety and efficacy of Lantus have been established in adolescents and children of 6 years and above. In children, efficacy and safety of Lantus have only been demonstrated when given in the evening. Due to limited experience on the efficacy and safety of Lantus in children below the age of 6 years, Lantus should only be used in this age group under careful medical supervision.

Transition from other insulins to Lantus

When changing from a treatment regimen with an intermediate or long acting insulin to a regimen with Lantus, 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 agents medicinal products)

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 Lantus should reduce their daily dose of basal insulin by 20-30% during the first weeks of treatment.

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.

As with other insulin analogues, patients with high insulin doses because of antibodies to human insulin may experience an improved insulin response with Lantus.

Close metabolic monitoring is recommended during the transition and in the initial weeks thereafter.

With improved metabolic control and resulting increase in insulin sensitivity a further adjustment in doseage 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).

METHOD OF ADMINISTRATION

Lantus is administered subcutaneously.

Lantus should not be administered intravenously. The prolonged duration of action of Lantus 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 Lantus. Injection sites must be rotated within a given injection area from one injection to the next.

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

Before using the pre-filled pen Solostar or Optiset, the Instructions for Use included in the Package Leaflet must be read carefully (see section 6.6).

For further details on handling, see section 6.6.

~~Due to limited experience the efficacy and safety of Lantus could not be assessed in the following groups of patients: patients with impaired liver function or patients with moderate/severe renal impairment (see section 4.4).~~

4.3 Contra-indications

Hypersensitivity to the active substance or to any of the excipients.

4.4 Special warnings and special precautions for use

Lantus is not the insulin of choice for the treatment of diabetic ketoacidosis. Instead, regular insulin administered intravenously is recommended in such cases.

~~Safety and efficacy of Lantus have been established in adolescents and children of 6 years and above.~~

~~Due to limited experience the efficacy and safety of Lantus could not be assessed in children below 6 years of age, in patients with impaired liver function or in patients with moderate/severe renal impairment (see section 4.2).~~

~~In patients with renal impairment, insulin requirements may be diminished due to reduced insulin metabolism. In the elderly, progressive deterioration of renal function may lead to a steady decrease in insulin requirements.~~

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

In case of insufficient glucose control or a tendency to hyper- or hypoglycaemic episodes, the patient's adherence to the prescribed treatment regimen, injection sites and proper injection technique and all other relevant factors must be reviewed before dose adjustment is considered.

Transferring **Switching** a patient to another type or brand of insulin should be done under strict medical supervision and may require change in dose. Changes in strength, brand (manufacturer), type (regular, NPH, lente, long-acting, etc.), origin (animal, human, human insulin analogue) and/or method of manufacture may result in the need for a change in dose.

Insulin administration may cause insulin antibodies to form. In rare cases, the presence of such insulin antibodies may necessitate adjustment of the insulin dose in order to correct a tendency to hyper- or hypoglycaemia. (See section 4.8)

Hypoglycaemia

The time of occurrence of hypoglycaemia depends on the action profile of the insulins used and may, therefore, change when the treatment regimen is changed. Due to more sustained basal insulin supply with Lantus, less nocturnal but more early morning hypoglycaemia can be expected.

Particular caution should be exercised, and intensified blood glucose monitoring is advisable in patients in whom hypoglycaemic episodes might be of particular clinical relevance, such as in patients with significant stenoses of the coronary arteries or of the blood vessels supplying the brain (risk of cardiac or cerebral complications of hypoglycaemia) as well as in patients with proliferative retinopathy, particularly if not treated with photocoagulation (risk of transient amaurosis following hypoglycaemia).

Patients should be aware of circumstances where warning symptoms of hypoglycaemia are diminished. The warning symptoms of hypoglycaemia may be changed, be less pronounced or be absent in certain risk groups. These include patients:

- in whom glycaemic control is markedly improved,
- in whom hypoglycaemia develops gradually,
- who are elderly,
- after transfer from animal insulin to human insulin,
- in whom an autonomic neuropathy is present,
- with a long history of diabetes,
- suffering from a psychiatric illness,
- receiving concurrent treatment with certain other medicinal products (see section 4.5).

Such situations may result in severe hypoglycaemia (and possibly loss of consciousness) prior to the patient's awareness of hypoglycaemia.

The prolonged effect of subcutaneous insulin glargine may delay recovery from hypoglycaemia.

If normal or decreased values for glycated haemoglobin are noted, the possibility of recurrent, unrecognised (especially nocturnal) episodes of hypoglycaemia must be considered.

Adherence of the patient to the dosage and dietary regimen, correct insulin administration and awareness of hypoglycaemia symptoms are essential to reduce the risk of hypoglycaemia. Factors increasing the susceptibility to hypoglycaemia require particularly close monitoring and may necessitate dose adjustment. These include:

- change in the injection area,
- improved insulin sensitivity (by, e.g., removal of stress factors),
- unaccustomed, increased or prolonged physical activity,
- intercurrent illness (e.g. vomiting, diarrhoea),
- inadequate food intake,

- missed meals,
- alcohol consumption,
- certain uncompensated endocrine disorders, (e.g. in hypothyroidism and in anterior pituitary or adrenocortical insufficiency),
- concomitant treatment with certain other medicinal products.

Intercurrent illness

Intercurrent illness requires intensified metabolic monitoring. In many cases urine tests for ketones are indicated, and often it is necessary to adjust the insulin dose. The insulin requirement is often increased. Patients with type 1 diabetes must continue to consume at least a small amount of carbohydrates on a regular basis, even if they are able to eat only little or no food, or are vomiting etc. and they must never omit insulin entirely.

Pens to be used with Lantus cartridges

The Lantus cartridges should only be used with the following pens: OptiPen, KlikSTAR, Tactipen and Autopen 24 and should not be used with any other reusable pen as the dosing accuracy has only been established with the listed pens.

Handling of the pen

Before using the pre-filled pen SoloStar, or Optiset the Instructions for Use included in the Package Leaflet must be read carefully. SoloStar or Optiset has to be used as recommended in these Instructions for Use (see section 6.6).

Medication errors

Medication errors have been reported in which other insulins, particularly short-acting insulins, have been accidentally administered instead of insulin glargine. Insulin label must always be checked before each injection to avoid medication errors between insulin glargine and other insulins.

Combination of Lantus with pioglitazone

Cases of cardiac failure have been reported when pioglitazone was used in combination with insulin, especially in patients with risk factors for development of cardiac heart failure. This should be kept in mind if treatment with the combination of pioglitazone and Lantus is considered. If the combination is used, patients should be observed for signs and symptoms of heart failure, weight gain and oedema.

Pioglitazone should be discontinued if any deterioration in cardiac symptoms occurs.

4.5 Interaction with other medicinal products and other forms of interaction

A number of substances affect glucose metabolism and may require dose adjustment of insulin glargine.

Substances that may enhance the blood-glucose-lowering effect and increase susceptibility to hypoglycaemia include oral antidiabetic agents medicinal products, angiotensin converting enzyme (ACE) inhibitors, disopyramide, fibrates, fluoxetine, monoamine oxidase (MAO) inhibitors, pentoxifylline, propoxyphene, salicylates and sulfonamide antibiotics.

Substances that may reduce the blood-glucose-lowering effect include corticosteroids, danazol, diazoxide, diuretics, glucagon, isoniazid, oestrogens and progestogens, phenothiazine derivatives, somatropin, sympathomimetic agents medicinal products (e.g. epinephrine [adrenaline], salbutamol, terbutaline), thyroid hormones, atypical antipsychotic medicinal products (e.g. olanzapine and clozapine) and protease inhibitors.

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 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 trials are available. A limited number of exposed pregnancies from Post Marketing Surveillance indicate no adverse effects of insulin glargine on pregnancy or on the health of the foetus and newborn child. To date, no other relevant epidemiological data are available.~~

~~Animal studies do not indicate direct harmful effects with respect to pregnancy, embryonal /foetal development, parturition or postnatal development (see section 5.3).~~

~~The available clinical data is insufficient to exclude a risk. The use of Lantus may be considered in pregnancy, if necessary.~~

~~It is essential for patients with pre-existing or gestational diabetes to maintain good metabolic control throughout pregnancy. 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.~~

Lactation

~~Lactating women may require adjustments in insulin dose and diet.~~

Pregnancy

For insulin glargine no clinical data on exposed pregnancies from controlled clinical trials are available. A moderate amount of data on pregnant women (between 300-1000 pregnancy outcomes) exposed to marketed insulin glargine indicate no adverse effects of insulin glargine on pregnancy and no malformative nor feto/neonatal toxicity of insulin glargine.

Animal data do not indicate reproductive toxicity.

The use of Lantus may be considered during pregnancy, if necessary.

It is essential for patients with pre-existing or gestational diabetes to maintain good metabolic control throughout pregnancy. 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.

Breastfeeding

It is unknown whether insulin glargine is excreted in human milk. No metabolic effects of ingested insulin glargine on the breastfed newborn/infant are anticipated since insulin glargine as a peptide is digested into aminoacids in the human gastrointestinal tract. Breastfeeding women may require adjustments in insulin dose and diet.

Fertility

Animal studies 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 or hyperglycaemia or, for example, as a result of visual impairment. 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 symptoms of hypoglycaemia or have frequent episodes of hypoglycaemia. It should be considered whether it is advisable to drive or operate machinery in these circumstances.

4.8 Undesirable effects

Hypoglycaemia

Hypoglycaemia, in general the most frequent **adverse reaction** ~~undesirable effect~~ of insulin therapy, may occur if the insulin dose is too high in relation to the insulin requirement.

The following related adverse reactions from clinical investigations **are** ~~were~~ listed below by system organ class and in order of decreasing incidence (very common: $\geq 1/10$; common: $\geq 1/100$ to $< 1/10$; uncommon: $\geq 1/1,000$ to $< 1/100$; rare: $\geq 1/10,000$ to $< 1/1,000$; very rare: $< 1/10,000$).

Within each frequency grouping, **adverse reactions** ~~undesirable effects~~ are presented in order of decreasing seriousness.

MedDRA system organ classes	Very common	Common	Uncommon	Rare	Very rare
Immune system disorders				Allergic reactions	
Metabolism and nutrition disorders	Hypoglycaemia				
Nervous system disorders					Dysgeusia
Eye disorders				Visual impairment Retinopathy	
Skin and subcutaneous tissue disorders		Lipohypertrophy	Lipoatrophy		

Musculoskeletal and connective tissue disorders					Myalgia
General disorders and administration site conditions		Injection site reactions		Oedema	

Metabolism and nutrition disorders

Very common: Hypoglycaemia

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.

Immune system disorders

Rare: Allergic reaction

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, angioedema, bronchospasm, hypotension and shock, and may be life-threatening.

Insulin administration may cause insulin antibodies to form. In clinical studies, antibodies that cross-react with human insulin and insulin glargine were observed with the same frequency in both NPH-Insulin and insulin glargine treatment groups. In rare cases, the presence of such insulin antibodies may necessitate adjustment of the insulin dose in order to correct a tendency to hyper- or hypoglycaemia.

~~Nervous system disorders:~~

Very rare: Dysgeusia

Eyes disorders

Rare: Visual impairment

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

Rare: Retinopathy

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

As with any insulin therapy, 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.

Common: Lipohypertrophy
Uncommon: Lipoatrophy

Musculoskeletal and connective tissue disorders

Very rare: Myalgia

General disorders and administration site conditions

Common: Injection site reactions

Injection site Such 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.

Rare: Oedema

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 patients** (≤ 18 years of age) is similar to the safety profile for **adults patients > 18 years**.

The adverse **reaction event** reports received from **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 patients** (≤ 18 years of age) than in **adults patients > 18 years**. No clinical study safety data are available in patients below 6 years of age.

4.9 Overdose

Symptoms

Insulin overdose may lead to severe and sometimes long-term and life-threatening hypoglycaemia.

Management

Mild episodes of hypoglycaemia can usually be treated with oral carbohydrates. Adjustments in **dose** **age** of the medicinal product, meal patterns, or physical activity may be needed.

More severe episodes with coma, seizure, or neurologic impairment may be treated with intramuscular/subcutaneous glucagon or concentrated intravenous glucose. Sustained carbohydrate intake and observation may be necessary because hypoglycaemia may recur after apparent clinical recovery.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: **Antidiabetic agent** **Drugs used in diabetes**. Insulins and analogues for injection, long-acting. ATC Code: A10A E04.

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 Lantus 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 receptor binding: Insulin glargine is very similar to human insulin with respect to insulin receptor binding kinetics. It can, therefore, be considered to mediate the same type of effect via the insulin receptor as insulin.

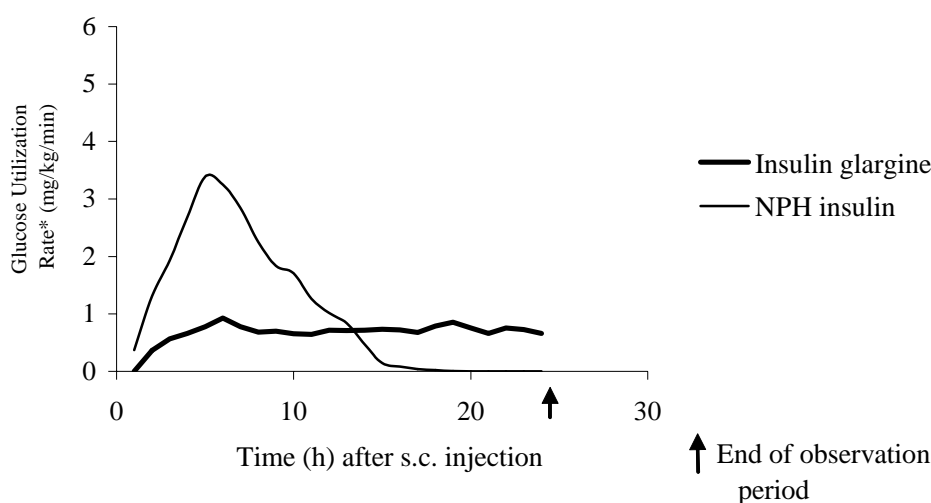
The primary activity of insulin, including insulin glargine, is regulation of glucose metabolism. Insulin and its analogues lower blood glucose levels by stimulating peripheral glucose uptake, especially by skeletal muscle and fat, and by inhibiting hepatic glucose production. Insulin inhibits lipolysis in the adipocyte, inhibits proteolysis and enhances protein synthesis.

In clinical pharmacology studies, intravenous insulin glargine and human insulin have been shown to be equipotent when given at the same doses. As with all insulins, the time course of action of insulin glargine may be affected by physical activity and other variables.

In euglycaemic clamp studies in healthy subjects or in patients with type 1 diabetes, the onset of action of subcutaneous insulin glargine was slower than with human NPH insulin, its effect profile was smooth and peakless, and the duration of its effect was prolonged.

The following graph shows the results from a study in patients:

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)

The longer duration of action of 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.

In a clinical study, symptoms of hypoglycaemia or counter-regulatory hormone responses were similar after intravenous insulin glargine and human insulin both in healthy volunteers and patients with type 1 diabetes.

Effects of insulin glargine (once daily) on diabetic retinopathy were evaluated in an open-label 5-year NPH controlled study (NPH given bid) in 1024 type 2 diabetic patients in which progression of retinopathy by 3 or more steps on the Early Treatment Diabetic Retinopathy Study (ETDRS) scale was investigated by fundus photography. No significant difference was seen in the progression of diabetic retinopathy when insulin glargine was compared to NPH insulin.

Paediatric population

In a randomised, controlled clinical study, paediatric patients (age range 6 to 15 years) with type 1 diabetes (n = 349) were treated for 28 weeks with a basal-bolus insulin regimen where regular human insulin was used before each meal. Insulin glargine was administered once daily at bedtime and NPH human insulin was administered once or twice daily. Similar effects on glycohemoglobin and the incidence of symptomatic hypoglycemia were observed in both treatment groups, however fasting plasma glucose decreased more from baseline in the insulin glargine group than in the NPH group.

There was less severe hypoglycaemia in the insulin glargine group as well. One hundred forty three of the patients treated with insulin glargine in this study continued treatment with insulin glargine in an uncontrolled extension study with mean duration of follow-up of 2 years. No new safety signals were seen during this extended treatment with insulin glargine.

A crossover study comparing insulin glargine plus lispro insulin to NPH plus regular human insulin (each treatment administered for 16 weeks in random order) in 26 adolescent type 1 diabetic patients aged 12 to 18 years was also performed. As in the paediatric study described above, fasting plasma glucose reduction from baseline was greater in the insulin glargine group than in the NPH group. HbA1c changes from baseline were similar between treatment groups; however blood glucose values recorded overnight were significantly higher in the insulin glargine/ lispro group than the NPH/regular group, with a mean nadir of 5.4 mM vs 4.1 mM. Correspondingly, the incidences of nocturnal hypoglycaemia were 32 % in the insulin glargine / lispro group vs 52 % in the NPH / regular group.

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.

In man, insulin glargine is partly degraded in the subcutaneous tissue at the carboxyl terminus of the Beta chain with formation of the active metabolites 21^A-Gly-insulin and 21^A -Gly-des-30^B-Thr-insulin. Unchanged insulin glargine and degradation products are also present in the plasma.

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.

Paediatric population

No specific pharmacokinetics study in children or adolescents was conducted.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on 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, hydrochloric acid, sodium hydroxide, water for injections.

10 ml vial also contains polysorbate 20.

6.2 Incompatibilities

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

It is important to ensure that syringes do not contain traces of any other material.

6.3 Shelf-life

Cartridge , Cartridge for OptiClik

3 years.

Shelf-life after first use of the cartridge:

The medicinal product may be stored for a maximum of 4 weeks not above 25°C away from direct heat or direct light. The pen containing a cartridge must not be stored in the refrigerator.

The pen cap must be put back on the pen after each injection in order to protect from light.

Vials

2 years

Shelf-life after first use of the vial:

The medicinal product may be stored for a maximum of 4 weeks not above 25°C away from direct heat or direct light. Keep the vial in the outer carton in order to protect from light.

It is recommended that the date of the first use from the vial be noted on the label.

Pre-filled pen (Optiset , Solostar)

3 years.

Shelf life after first use of the pen:

The medicinal product may be stored for a maximum of 4 weeks not above 25°C away from direct heat or direct

light. Pens in use must not be stored in the refrigerator.

The pen cap must be put back on the pen after each injection in order to protect from light.

6.4 Special precautions for storage

Vials

Unopened vials

Store in a refrigerator (2°C-8°C).

Do not freeze.

Do not put Lantus next to the freezer compartment or a freezer pack.

Keep the vial in the outer carton in order to protect from light.

Opened vials

For storage precautions, see section 6.3.

Cartridges, cartridge for OptiClik

Unopened cartridges

Store in a refrigerator (2°C-8°C).

Do not freeze.

Do not put Lantus next to the freezer compartment or a freezer pack.

Keep the cartridge in the outer carton in order to protect from light.

In use cartridges

For storage precautions, see section 6.3.

Pre-filled pens

Not in-use pens

Store in a refrigerator (2°C-8°C).

Do not freeze.

Do not put Lantus next to the freezer compartment or a freezer pack.

Keep the prefilled pen in the outer carton in order to protect from light.

In-use pens

For storage precautions, see section 6.3.

6.5 Special precautions for disposal and other handling

Lantus 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. (see section 4.4)

Vial

Inspect the vial 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 Lantus is a solution, it does not require resuspension before use.

Cartridge, cartridge for OptiClik

Insulin pen

The Lantus cartridges are to be used only in conjunction with ~~an insulin pen such as~~ OptiPen, Autopen 24 or Tactipen (see section 4.4) ~~and other pens suitable for Lantus cartridges~~. Not all of these pens may be marketed in Israel.

The pen should be used ~~and~~ as recommended in the information provided by the device manufacturer.

The manufacturer's instructions for using the pen must be followed carefully for loading the cartridge, attaching the needle, and administering the insulin injection.

If the insulin pen is damaged or not working properly (due to mechanical defects) it has to be discarded, and a new insulin pen has to be used.

If the pen malfunctions (see instructions for using the pen), the solution may be drawn from the cartridge into a syringe (suitable for an insulin with 100 Units/ml) and injected.

Cartridge

Before insertion into the pen, the cartridge must be stored at room temperature for 1 to 2 hours.

Inspect the cartridge 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 Lantus is a solution, it does not require resuspension before use.

Air bubbles must be removed from the cartridge before injection (see instructions for using the pen). Empty cartridges must not be refilled.

Cartridge for OptiClik

The cartridges for OptiClik are to be used in conjunction with OptiClik only and as recommended in the information provided by the device manufacturer.

The manufacturer's instructions for using the pen must be followed carefully for loading the cartridge, attaching the needle, and administering the insulin injection.

If OptiClik is damaged or not working properly (due to mechanical defects) it has to be discarded, and a new OptiClik has to be used.

Before insertion into the pen, the cartridge must be stored at room temperature for 1 to 2 hours. Inspect the cartridge before use. It must only be used if the cartridge is intact and the solution is clear, colourless, with no solid particles visible, and if it is of water-like consistency. Since Lantus is a solution, it does not require resuspension before use. Air bubbles must be removed from the cartridge before injection (see instructions for using the pen). Empty cartridges must not be refilled.

If the pen malfunctions (see instructions for using the pen), the solution may be drawn from the cartridge into a syringe (suitable for an insulin with 100 IU/ml) and injected.

Pre-filled pen - Optiset or Solostar

Before first use, the pen must be stored at room temperature for 1 to 2 hours. Inspect the cartridge 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 Lantus is a solution, it does not require resuspension before use. Empty pens must never be reused and must be properly discarded. To prevent the possible transmission of disease, each pen must be used by one patient only.

Handling of the pen

The Instructions for Use included in the Package Leaflet must be read carefully before using OptiSet or SoloSTAR.

MANUFACTURER:

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IMPORTER:

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