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Rx Only

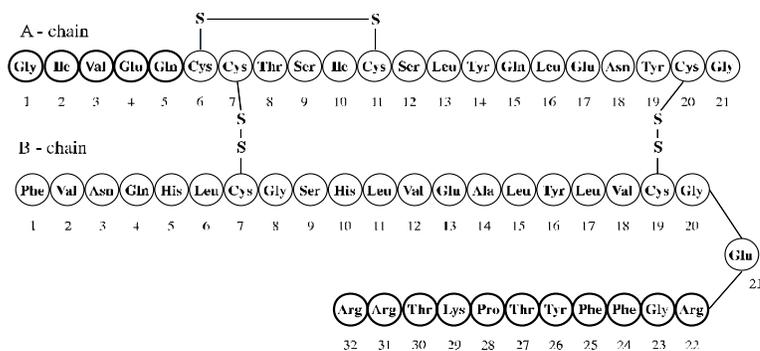
LANTUS[®]

(insulin glargine [rDNA origin] injection)

LANTUS[®] must NOT be diluted or mixed with any other insulin or solution.

DESCRIPTION

LANTUS[®] (insulin glargine [rDNA origin] injection) is a sterile solution of insulin glargine for use as an injection. Insulin glargine is a recombinant human insulin analog that is a long-acting (up to 24-hour duration of action), parenteral blood-glucose-lowering agent. (See CLINICAL PHARMACOLOGY). LANTUS is produced by recombinant DNA technology utilizing a non-pathogenic laboratory strain of *Escherichia coli* (K12) as the production organism. Insulin glargine differs from human insulin in that the amino acid asparagine at position A21 is replaced by glycine and two arginines are added to the C-terminus of the B-chain. Chemically, it is 21^A-Gly-30^Ba-L-Arg-30^Bb-L-Arg-human insulin and has the empirical formula C₂₆₇H₄₀₄N₇₂O₇₈S₆ and a molecular weight of 6063. It has the following structural formula:



LANTUS consists of insulin glargine dissolved in a clear aqueous fluid. Each milliliter of LANTUS (insulin glargine injection) contains 100 IU (3.6378 mg) insulin glargine.

Inactive ingredients for the 10 mL vial are 30 mcg zinc, 2.7 mg m-cresol, 20 mg glycerol 85%, 20 mcg polysorbate 20, and water for injection.

Inactive ingredients for the 3 mL cartridge are 30 mcg zinc, 2.7 mg m-cresol, 20 mg glycerol 85%, and water for injection.

The pH is adjusted by addition of aqueous solutions of hydrochloric acid and sodium hydroxide. LANTUS has a pH of approximately 4.

CLINICAL PHARMACOLOGY

Mechanism of Action:

The primary activity of insulin, including insulin glargine, is regulation of glucose metabolism. Insulin and its analogs lower blood glucose levels by stimulating peripheral glucose uptake,

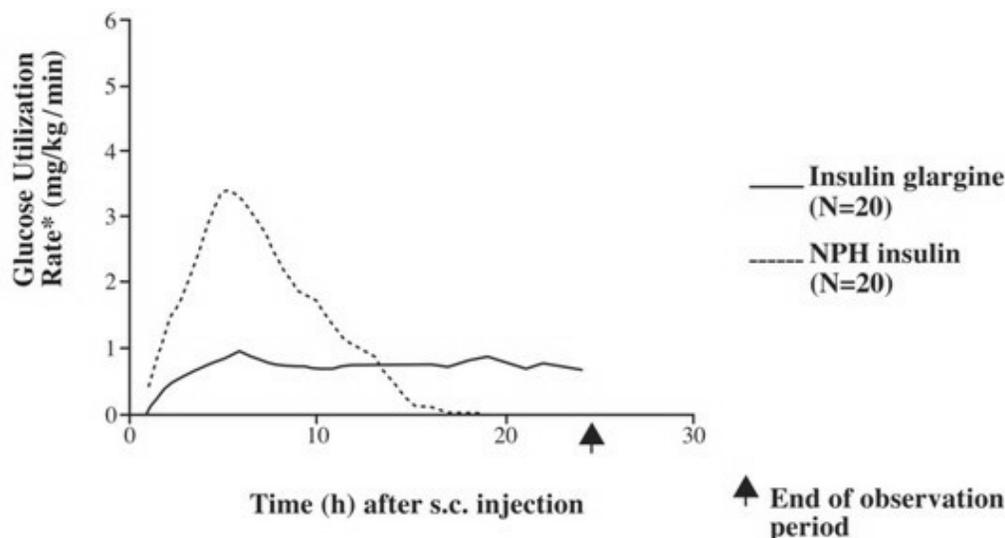
especially by skeletal muscle and fat, and by inhibiting hepatic glucose production. Insulin inhibits lipolysis in the adipocyte, inhibits proteolysis, and enhances protein synthesis.

Pharmacodynamics:

Insulin glargine is a human insulin analog that has been designed to have low aqueous solubility at neutral pH. At pH 4, as in the LANTUS injection solution, it is completely soluble. After injection into the subcutaneous tissue, the acidic solution is neutralized, leading to formation of microprecipitates from which small amounts of insulin glargine are slowly released, resulting in a relatively constant concentration/time profile over 24 hours with no pronounced peak. This profile allows once-daily dosing as a patient's basal insulin.

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 (up to 24 hours) of LANTUS is directly related to its slower rate of absorption and supports once-daily subcutaneous administration. The time course of action of insulins, including LANTUS, may vary between individuals and/or within the same individual.

Pharmacokinetics:

Absorption and Bioavailability. After subcutaneous injection of insulin glargine in healthy subjects and in patients with diabetes, the insulin serum concentrations indicated a slower, more prolonged absorption and a relatively constant concentration/time profile over 24 hours with no pronounced peak in comparison to NPH human insulin. Serum insulin concentrations were thus consistent with the time profile of the pharmacodynamic activity of insulin glargine.

After subcutaneous injection of 0.3 IU/kg insulin glargine in patients with type 1 diabetes, a relatively constant concentration/time profile has been demonstrated. The duration of action after abdominal, deltoid, or thigh subcutaneous administration was similar.

Metabolism. A metabolism study in humans indicates that insulin glargine is partly metabolized at the carboxyl terminus of the B chain in the subcutaneous depot to form two active metabolites with in vitro activity similar to that of insulin, M1 (21^A-Gly-insulin) and M2 (21^A-Gly-des-30^B-Thr-insulin). Unchanged drug and these degradation products are also present in the circulation.

Special Populations:

Age, Race, and Gender. Information on the effect of age, race, and gender on the pharmacokinetics of LANTUS is not available. However, in controlled clinical trials in adults (n=3890) and a controlled clinical trial in pediatric patients (n=349), subgroup analyses based on age, race, and gender did not show differences in safety and efficacy between insulin glargine and NPH human insulin.

Smoking. The effect of smoking on the pharmacokinetics/pharmacodynamics of LANTUS has not been studied.

Pregnancy. The effect of pregnancy on the pharmacokinetics and pharmacodynamics of LANTUS has not been studied (see PRECAUTIONS, Pregnancy).

Obesity. In controlled clinical trials, which included patients with Body Mass Index (BMI) up to and including 49.6 kg/m², subgroup analyses based on BMI did not show any differences in safety and efficacy between insulin glargine and NPH human insulin.

Renal Impairment. The effect of renal impairment on the pharmacokinetics of LANTUS has not been studied. However, some studies with human insulin have shown increased circulating levels of insulin in patients with renal failure. Careful glucose monitoring and dose adjustments of insulin, including LANTUS, may be necessary in patients with renal dysfunction (see PRECAUTIONS, Renal Impairment).

Hepatic Impairment. The effect of hepatic impairment on the pharmacokinetics of LANTUS has not been studied. However, some studies with human insulin have shown increased circulating levels of insulin in patients with liver failure. Careful glucose monitoring and dose adjustments of insulin, including LANTUS, may be necessary in patients with hepatic dysfunction (see PRECAUTIONS, Hepatic Impairment).

Clinical Studies

The safety and effectiveness of insulin glargine given once-daily at bedtime was compared to that of once-daily and twice-daily NPH human insulin in open-label, randomized, active-control,

parallel studies of 2327 adult patients and 349 pediatric patients with type 1 diabetes mellitus and 1563 adult patients with type 2 diabetes mellitus (see Tables 1-3). In general, the reduction in glycated hemoglobin (HbA1c) with LANTUS was similar to that with NPH human insulin. The overall rates of hypoglycemia did not differ between patients with diabetes treated to LANTUS compared with NPH human insulin.

Type 1 Diabetes—Adult (see Table 1). In two large, randomized, controlled clinical studies (Studies A and B), patients with type 1 diabetes (Study A; n=585, Study B; n=534) were randomized to basal-bolus treatment with LANTUS once daily at bedtime or to NPH human insulin once or twice daily and treated for 28 weeks. Regular human insulin was administered before each meal. LANTUS was administered at bedtime. NPH human insulin was administered once daily at bedtime or in the morning and at bedtime when used twice daily. In one large, randomized, controlled clinical study (Study C), patients with type 1 diabetes (n=619) were treated for 16 weeks with a basal-bolus insulin regimen where insulin lispro was used before each meal. LANTUS was administered once daily at bedtime and NPH human insulin was administered once or twice daily. In these studies, LANTUS and NPH human insulin had a similar effect on glycohemoglobin with a similar overall rate of hypoglycemia.

Table 1: Type 1 Diabetes Mellitus–Adult

	<u>Study A</u>		<u>Study B</u>		<u>Study C</u>	
	28 weeks Regular insulin		28 weeks Regular insulin		16 weeks Insulin lispro	
	<u>LANTUS</u>	<u>NPH</u>	<u>LANTUS</u>	<u>NPH</u>	<u>LANTUS</u>	<u>NPH</u>
Treatment duration						
Treatment in combination with						
Number of subjects treated	292	293	264	270	310	309
HbA1c						
Endstudy mean	8.13	8.07	7.55	7.49	7.53	7.60
Adj. mean change from baseline	+0.21	+0.10	-0.16	-0.21	-0.07	-0.08
LANTUS – NPH	+0.11		+0.05		+0.01	
95% CI for Treatment difference	(-0.03; +0.24)		(-0.08; +0.19)		(-0.11; +0.13)	
Basal insulin dose						
Endstudy mean	19.2	22.8	24.8	31.3	23.9	29.2
Mean change from baseline	-1.7	-0.3	-4.1	+1.8	-4.5	+0.9
Total insulin dose						
Endstudy mean	46.7	51.7	50.3	54.8	47.4	50.7
Mean change from baseline	-1.1	-0.1	+0.3	+3.7	-2.9	+0.3
Fasting blood glucose (mg/dL)						
Endstudy mean	146.3	150.8	147.8	154.4	144.4	161.3
Adj. mean change from baseline	-21.1	-16.0	-20.2	-16.9	-29.3	-11.9

Type 1 Diabetes–Pediatric (see Table 2). In a randomized, controlled clinical study (Study D), pediatric 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. LANTUS was administered once daily at bedtime and NPH human insulin was administered once or twice daily. Similar effects on glycohemoglobin and the incidence of hypoglycemia were observed in both treatment groups.

Table 2: Type 1 Diabetes Mellitus–Pediatric

Treatment duration Treatment in combination with	Study D 28 weeks Regular insulin	
	<u>LANTUS</u>	<u>NPH</u>
Number of subjects treated	174	175
HbA1c		
Endstudy mean	8.91	9.18
Adj. mean change from baseline	+0.28	+0.27
LANTUS – NPH		+0.01
95% CI for Treatment difference		(-0.24; +0.26)
Basal insulin dose		
Endstudy mean	18.2	21.1
Mean change from baseline	-1.3	+2.4
Total insulin dose		
Endstudy mean	45.0	46.0
Mean change from baseline	+1.9	+3.4
Fasting blood glucose (mg/dL)		
Endstudy mean	171.9	182.7
Adj. mean change from baseline	-23.2	-12.2

Type 2 Diabetes–Adult (see Table 3). In a large, randomized, controlled clinical study (Study E) (n=570), LANTUS was evaluated for 52 weeks as part of a regimen of combination therapy with insulin and oral antidiabetes agents (a sulfonylurea, metformin, acarbose, or combinations of these drugs). LANTUS administered once daily at bedtime was as effective as NPH human insulin administered once daily at bedtime in reducing glycohemoglobin and fasting glucose. There was a low rate of hypoglycemia that was similar in LANTUS and NPH human insulin treated patients. In a large, randomized, controlled clinical study (Study F), in patients with type 2 diabetes not using oral antidiabetes agents (n=518), a basal-bolus regimen of LANTUS once daily at bedtime or NPH human insulin administered once or twice daily was evaluated for 28 weeks. Regular human insulin was used before meals as needed. LANTUS had similar effectiveness as either once- or twice-daily NPH human insulin in reducing glycohemoglobin and fasting glucose with a similar incidence of hypoglycemia.

Table 3: Type 2 Diabetes Mellitus–Adult

Treatment duration Treatment in combination with	<u>Study E</u> 52 weeks Oral agents		<u>Study F</u> 28 weeks Regular insulin	
	<u>LANTUS</u>	<u>NPH</u>	<u>LANTUS</u>	<u>NPH</u>
Number of subjects treated	289	281	259	259
HbA1c				
Endstudy mean	8.51	8.47	8.14	7.96
Adj. mean change from baseline	-0.46	-0.38	-0.41	-0.59
LANTUS – NPH	-0.08		+0.17	
95% CI for Treatment difference	(-0.28; +0.12)		(-0.00; +0.35)	
Basal insulin dose				
Endstudy mean	25.9	23.6	42.9	52.5
Mean change from baseline	+11.5	+9.0	-1.2	+7.0
Total insulin dose				
Endstudy mean	25.9	23.6	74.3	80.0
Mean change from baseline	+11.5	+9.0	+10.0	+13.1
Fasting blood glucose (mg/dL)				
Endstudy mean	126.9	129.4	141.5	144.5
Adj. mean change from baseline	-49.0	-46.3	-23.8	-21.6

LANTUS Flexible Daily Dosing

The safety and efficacy of LANTUS administered pre-breakfast, pre-dinner, or at bedtime were evaluated in a large, randomized, controlled clinical study, in patients with type 1 diabetes (study G, n=378). Patients were also treated with insulin lispro at mealtime. LANTUS administered at different times of the day resulted in similar reductions in glycated hemoglobin compared to that with bedtime administration (see Table 4). In these patients, data are available from 8-point home glucose monitoring. The maximum mean blood glucose level was observed just prior to injection of LANTUS regardless of time of administration, i.e. pre-breakfast, pre-dinner, or bedtime.

In this study, 5% of patients in the LANTUS-breakfast arm discontinued treatment because of lack of efficacy. No patients in the other two arms discontinued for this reason. Routine monitoring during this trial revealed the following mean changes in systolic blood pressure: pre-breakfast group, 1.9 mm Hg; pre-dinner group, 0.7 mm Hg; pre-bedtime group, -2.0 mm Hg.

The safety and efficacy of LANTUS administered pre-breakfast or at bedtime were also evaluated in a large, randomized, active-controlled clinical study (Study H, n=697) in type 2 diabetes patients no longer adequately controlled on oral agent therapy. All patients in this study also received AMARYL® (glimepiride) 3 mg daily. LANTUS given before breakfast was at least as effective in lowering glycated hemoglobin A1c (HbA1c) as LANTUS given at bedtime or NPH human insulin given at bedtime (see Table 4).

Table 4: Flexible LANTUS Daily Dosing in Type 1 (Study G) and Type 2 (Study H) Diabetes Mellitus

Treatment duration Treatment in combination with:	<u>Study G</u> 24 weeks Insulin lispro			<u>Study H</u> 24 weeks AMARYL® (glimepiride)		
	<u>LANTUS</u> <u>Breakfast</u>	<u>LANTUS</u> <u>Dinner</u>	<u>LANTUS</u> <u>Bedtime</u>	<u>LANTUS</u> <u>Breakfast</u>	<u>LANTUS</u> <u>Bedtime</u>	<u>NPH</u> <u>Bedtime</u>
Number of subjects treated*	112	124	128	234	226	227

HbA1c						
Baseline mean	7.56	7.53	7.61	9.13	9.07	9.09
Endstudy mean	7.39	7.42	7.57	7.87	8.12	8.27
Mean change from baseline	-0.17	-0.11	-0.04	-1.26	-0.95	-0.83
Basal insulin dose (IU)						
Endstudy mean	27.3	24.6	22.8	40.4	38.5	36.8
Mean change from baseline	5.0	1.8	1.5			
Total insulin dose (IU)				NA**	NA	NA
Endstudy mean	53.3	54.7	51.5			
Mean change from baseline	1.6	3.0	2.3			

*Intent to treat **Not applicable

INDICATIONS AND USAGE

LANTUS is indicated for once-daily subcutaneous administration for the treatment of adult and pediatric patients with type 1 diabetes mellitus or adult patients with type 2 diabetes mellitus who require basal (long-acting) insulin for the control of hyperglycemia.

CONTRAINDICATIONS

LANTUS is contraindicated in patients hypersensitive to insulin glargine or the excipients.

WARNINGS

Hypoglycemia is the most common adverse effect of insulin, including LANTUS. As with all insulins, the timing of hypoglycemia may differ among various insulin formulations. Glucose monitoring is recommended for all patients with diabetes.

Any change of insulin should be made cautiously and only under medical supervision. Changes in insulin strength, timing of dosing, manufacturer, type (e.g., regular, NPH, or insulin analogs), species (animal, human), or method of manufacture (recombinant DNA versus animal-source insulin) may result in the need for a change in dosage. Concomitant oral antidiabetes treatment may need to be adjusted.

PRECAUTIONS

General:

LANTUS is not intended for intravenous administration. The prolonged duration of activity of insulin glargine is dependent on injection into subcutaneous tissue. Intravenous administration of the usual subcutaneous dose could result in severe hypoglycemia.

LANTUS must NOT be diluted or mixed with any other insulin or solution. If LANTUS is diluted or mixed, the solution may become cloudy, and the pharmacokinetic/pharmacodynamic profile (e.g., onset of action, time to peak effect) of LANTUS and/or the mixed insulin may be altered in an unpredictable manner. When LANTUS and regular human insulin were mixed immediately before injection in dogs, a delayed onset of action and time to maximum effect for regular human insulin was observed. The total bioavailability of the mixture was also slightly decreased compared to separate injections of LANTUS and regular human insulin. The relevance of these observations in dogs to humans is not known.

As with all insulin preparations, the time course of LANTUS action may vary in different individuals or at different times in the same individual and the rate of absorption is dependent on blood supply, temperature, and physical activity.

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

Hypoglycemia:

As with all insulin preparations, hypoglycemic reactions may be associated with the administration of LANTUS. Hypoglycemia is the most common adverse effect of insulins. Early warning symptoms of hypoglycemia may be different or less pronounced under certain conditions, such as long duration of diabetes, diabetes nerve disease, use of medications such as beta-blockers, or intensified diabetes control (see PRECAUTIONS, Drug Interactions). Such situations may result in severe hypoglycemia (and, possibly, loss of consciousness) prior to patients' awareness of hypoglycemia.

The time of occurrence of hypoglycemia depends on the action profile of the insulins used and may, therefore, change when the treatment regimen or timing of dosing is changed. Patients being switched from twice daily NPH insulin to once-daily LANTUS should have their initial LANTUS dose reduced by 20% from the previous total daily NPH dose to reduce the risk of hypoglycemia (see DOSAGE AND ADMINISTRATION, Changeover to LANTUS).

The prolonged effect of subcutaneous LANTUS may delay recovery from hypoglycemia.

In a clinical study, symptoms of hypoglycemia or counterregulatory hormone responses were similar after intravenous insulin glargine and regular human insulin both in healthy subjects and patients with type 1 diabetes.

Renal Impairment:

Although studies have not been performed in patients with diabetes and renal impairment, LANTUS requirements may be diminished because of reduced insulin metabolism, similar to observations found with other insulins (see CLINICAL PHARMACOLOGY, Special Populations).

Hepatic Impairment:

Although studies have not been performed in patients with diabetes and hepatic impairment, LANTUS requirements may be diminished due to reduced capacity for gluconeogenesis and reduced insulin metabolism, similar to observations found with other insulins (see CLINICAL PHARMACOLOGY, Special Populations).

Injection Site and Allergic Reactions:

As with any insulin therapy, lipodystrophy may occur at the injection site and delay insulin absorption. Other injection site reactions with insulin therapy include redness, pain, itching, hives, swelling, and inflammation. Continuous rotation of the injection site within a given area may help to reduce or prevent these reactions. Most minor reactions to insulins usually resolve in a few days to a few weeks.

Reports of injection site pain were more frequent with LANTUS than NPH human insulin (2.7% insulin glargine versus 0.7% NPH). The reports of pain at the injection site were usually mild and did not result in discontinuation of therapy.

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

Intercurrent Conditions:

Insulin requirements may be altered during intercurrent conditions such as illness, emotional disturbances, or stress.

Information for Patients:

LANTUS must only be used if the solution is clear and colorless with no particles visible (see DOSAGE AND ADMINISTRATION, Preparation and Handling).

Patients must be advised that LANTUS must NOT be diluted or mixed with any other insulin or solution (see PRECAUTIONS, General).

Patients should be instructed on self-management procedures including glucose monitoring, proper injection technique, and hypoglycemia and hyperglycemia management. Patients must be instructed on handling of special situations such as intercurrent conditions (illness, stress, or emotional disturbances), an inadequate or skipped insulin dose, inadvertent administration of an increased insulin dose, inadequate food intake, or skipped meals. Refer patients to the LANTUS “Patient Information” circular for additional information.

As with all patients who have diabetes, the ability to concentrate and/or react may be impaired as a result of hypoglycemia or hyperglycemia.

Patients with diabetes should be advised to inform their health care professional if they are pregnant or are contemplating pregnancy.

Drug Interactions:

A number of substances affect glucose metabolism and may require insulin dose adjustment and particularly close monitoring.

The following are examples of substances that may increase the blood-glucose-lowering effect and susceptibility to hypoglycemia: oral antidiabetes products, ACE inhibitors, disopyramide, fibrates, fluoxetine, MAO inhibitors, propoxyphene, salicylates, somatostatin analog (e.g., octreotide), sulfonamide antibiotics.

The following are examples of substances that may reduce the blood-glucose-lowering effect of insulin: corticosteroids, danazol, diuretics, sympathomimetic agents (e.g., epinephrine, albuterol, terbutaline), isoniazid, phenothiazine derivatives, somatropin, thyroid hormones, estrogens, progestogens (e.g., in oral contraceptives), protease inhibitors and atypical antipsychotic medications (e.g. olanzapine and clozapine).

Beta-blockers, clonidine, lithium salts, and alcohol may either potentiate or weaken the blood-glucose-lowering effect of insulin. Pentamidine may cause hypoglycemia, which may sometimes be followed by hyperglycemia.

In addition, under the influence of sympatholytic medicinal products such as beta-blockers, clonidine, guanethidine, and reserpine, the signs of hypoglycemia may be reduced or absent.

Carcinogenesis, Mutagenesis, Impairment of Fertility:

In mice and rats, standard two-year carcinogenicity studies with insulin glargine were performed at doses up to 0.455 mg/kg, which is for the rat approximately 10 times and for the mouse approximately 5 times the recommended human subcutaneous starting dose of 10 IU (0.008 mg/kg/day), based on mg/m². The findings in female mice were not conclusive due to excessive

mortality in all dose groups during the study. Histiocytomas were found at injection sites in male rats (statistically significant) and male mice (not statistically significant) in acid vehicle containing groups. These tumors were not found in female animals, in saline control, or insulin comparator groups using a different vehicle. The relevance of these findings to humans is unknown.

Insulin glargine was not mutagenic in tests for detection of gene mutations in bacteria and mammalian cells (Ames- and HGPRT-test) and in tests for detection of chromosomal aberrations (cytogenetics in vitro in V79 cells and in vivo in Chinese hamsters).

In a combined fertility and prenatal and postnatal study in male and female rats at subcutaneous doses up to 0.36 mg/kg/day, which is approximately 7 times the recommended human subcutaneous starting dose of 10 IU (0.008 mg/kg/day), based on mg/m², maternal toxicity due to dose-dependent hypoglycemia, including some deaths, was observed. Consequently, a reduction of the rearing rate occurred in the high-dose group only. Similar effects were observed with NPH human insulin.

Pregnancy:

Teratogenic Effects: Pregnancy Category C. Subcutaneous reproduction and teratology studies have been performed with insulin glargine and regular human insulin in rats and Himalayan rabbits. The drug was given to female rats before mating, during mating, and throughout pregnancy at doses up to 0.36 mg/kg/day, which is approximately 7 times the recommended human subcutaneous starting dose of 10 IU (0.008 mg/kg/day), based on mg/m². In rabbits, doses of 0.072 mg/kg/day, which is approximately 2 times the recommended human subcutaneous starting dose of 10 IU (0.008 mg/kg/day), based on mg/m², were administered during organogenesis. The effects of insulin glargine did not generally differ from those observed with regular human insulin in rats or rabbits. However, in rabbits, five fetuses from two litters of the high-dose group exhibited dilation of the cerebral ventricles. Fertility and early embryonic development appeared normal.

There are no well-controlled clinical studies of the use of insulin glargine in pregnant women. It is essential for patients with diabetes or a history of gestational diabetes to maintain good metabolic control before conception and throughout pregnancy. Insulin requirements may decrease during the first trimester, generally increase during the second and third trimesters, and rapidly decline after delivery. Careful monitoring of glucose control is essential in such patients. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers:

It is unknown whether insulin glargine is excreted in significant amounts in human milk. Many drugs, including human insulin, are excreted in human milk. For this reason, caution should be exercised when LANTUS is administered to a nursing woman. Lactating women may require adjustments in insulin dose and diet.

Pediatric Use:

Safety and effectiveness of LANTUS have been established in the age group 6 to 15 years with type 1 diabetes.

Geriatric Use:

In controlled clinical studies comparing insulin glargine to NPH human insulin, 593 of 3890 patients with type 1 and type 2 diabetes were 65 years and older. The only difference in safety or effectiveness in this subpopulation compared to the entire study population was an expected higher incidence of cardiovascular events in both insulin glargine and NPH human insulin-treated patients.

In elderly patients with diabetes, the initial dosing, dose increments, and maintenance dosage should be conservative to avoid hypoglycemic reactions. Hypoglycemia may be difficult to recognize in the elderly (see PRECAUTIONS, Hypoglycemia).

ADVERSE REACTIONS

The adverse events commonly associated with LANTUS include the following:

Body as a whole: allergic reactions (see PRECAUTIONS).

Skin and appendages: injection site reaction, lipodystrophy, pruritus, rash (see PRECAUTIONS).

Other: hypoglycemia (see WARNINGS and PRECAUTIONS).

In clinical studies in adult patients, there was a higher incidence of treatment-emergent injection site pain in LANTUS-treated patients (2.7%) compared to NPH insulin-treated patients (0.7%). The reports of pain at the injection site were usually mild and did not result in discontinuation of therapy. Other treatment-emergent injection site reactions occurred at similar incidences with both insulin glargine and NPH human insulin.

Retinopathy was evaluated in the clinical studies by means of retinal adverse events reported and fundus photography. The numbers of retinal adverse events reported for LANTUS and NPH treatment groups were similar for patients with type 1 and type 2 diabetes. Progression of retinopathy was investigated by fundus photography using a grading protocol derived from the Early Treatment Diabetic Retinopathy Study (ETDRS). In one clinical study involving patients with type 2 diabetes, a difference in the number of subjects with ≥ 3 -step progression in ETDRS scale over a 6-month period was noted by fundus photography (7.5% in LANTUS group versus 2.7% in NPH treated group). The overall relevance of this isolated finding cannot be determined due to the small number of patients involved, the short follow-up period, and the fact that this finding was not observed in other clinical studies.

OVERDOSAGE

An excess of insulin relative to food intake, energy expenditure, or both may lead to severe and sometimes long-term and life-threatening hypoglycemia. 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 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 reoccurrence of hypoglycemia.

DOSAGE AND ADMINISTRATION

LANTUS is a recombinant human insulin analog. Its potency is approximately the same as human insulin. It exhibits a relatively constant glucose-lowering profile over 24 hours that permits once-daily dosing.

LANTUS may be administered at any time during the day. LANTUS should be administered subcutaneously once a day at the same time every day. For patients adjusting timing of dosing with LANTUS, see **WARNINGS** and **PRECAUTIONS, Hypoglycemia**. LANTUS is not intended for intravenous administration (see **PRECAUTIONS**). Intravenous administration of the usual subcutaneous dose could result in severe hypoglycemia. The desired blood glucose levels as well as the doses and timing of antidiabetes medications must be determined individually. Blood glucose monitoring is recommended for all patients with diabetes. The prolonged duration of activity of LANTUS is dependent on injection into subcutaneous space.

As with all insulins, injection sites within an injection area (abdomen, thigh, or deltoid) must be rotated from one injection to the next.

In clinical studies, there was no relevant difference in insulin glargine absorption after abdominal, deltoid, or thigh subcutaneous administration. As for all insulins, the rate of absorption, and consequently the onset and duration of action, may be affected by exercise and other variables.

LANTUS is not the insulin of choice for the treatment of diabetes ketoacidosis. Intravenous short-acting insulin is the preferred treatment.

Pediatric Use:

LANTUS can be safely administered to pediatric patients ≥ 6 years of age. Administration to pediatric patients < 6 years has not been studied. Based on the results of a study in pediatric patients, the dose recommendation for changeover to LANTUS is the same as described for adults in **DOSAGE AND ADMINISTRATION, Changeover to LANTUS**.

Initiation of LANTUS Therapy:

In a clinical study with insulin naïve patients with type 2 diabetes already treated with oral antidiabetes drugs, LANTUS was started at an average dose of 10 IU once daily, and subsequently adjusted according to the patient's need to a total daily dose ranging from 2 to 100 IU.

Changeover to LANTUS:

If changing from a treatment regimen with an intermediate- or long-acting insulin to a regimen with LANTUS, the amount and timing of short-acting insulin or fast-acting insulin analog or the dose of any oral antidiabetes drug may need to be adjusted. In clinical studies, when patients were transferred from once-daily NPH human insulin or ultralente human insulin to once-daily LANTUS, the initial dose was usually not changed. However, when patients were transferred from twice-daily NPH human insulin to LANTUS once daily, to reduce the risk of hypoglycemia, the initial dose (IU) was usually reduced by approximately 20% (compared to total daily IU of NPH human insulin) and then adjusted based on patient response (see **PRECAUTIONS, Hypoglycemia**).

A program of close metabolic monitoring under medical supervision is recommended during transfer and in the initial weeks thereafter. The amount and timing of short-acting insulin or fast-acting insulin analog may need to be adjusted. This is particularly true for patients with acquired antibodies to human insulin needing high-insulin doses and occurs with all insulin analogs. Dose adjustment of LANTUS and other insulins or oral antidiabetes drugs may be required; for

example, if the patient's timing of dosing, weight or lifestyle changes, or other circumstances arise that increase susceptibility to hypoglycemia or hyperglycemia (see PRECAUTIONS, Hypoglycemia).

The dose may also have to be adjusted during intercurrent illness (see PRECAUTIONS, Intercurrent Conditions).

Preparation and Handling:

Parenteral drug products should be inspected visually prior to administration whenever the solution and the container permit. LANTUS must only be used if the solution is clear and colorless with no particles visible.

Mixing and diluting: LANTUS must NOT be diluted or mixed with any other insulin or solution (see PRECAUTIONS, General).

Vial: The syringes must not contain any other medicinal product or residue.

Cartridge system/SoloStar: If OptiClik[®], the Insulin Delivery Device used with the LANTUS cartridge system, or SoloStar, disposable insulin device, malfunctions, LANTUS may be drawn from the cartridge system or from SoloStar into a U-100 syringe and injected.

HOW SUPPLIED

LANTUS 100 units per mL (U-100) is available in the following package size:

10 mL vials (NDC 0088-2220-33)

3 mL cartridge system*, package of 5 (NDC 0088-2220-52)

*Cartridge systems are for use only in OptiClik[®] (Insulin Delivery Device)

3 mL SoloStar[®] disposable insulin device, package of 5 (NDC 0088-2220-60)

Needles are not included in the packs.

BD Ultra-Fine™ needles[†] to be used in conjunction with SoloStar and OptiClik are sold separately and are manufactured by BD.

Storage:

Unopened Vial/Cartridge system/SoloStar[®] disposable insulin device:

Unopened LANTUS vials, cartridge systems and SoloStar[®] should be stored in a refrigerator, 36°F - 46°F (2°C - 8°C). LANTUS should not be stored in the freezer and it should not be allowed to freeze. Discard if it has been frozen.

Open (In-Use) Vial:

Opened vials, whether or not refrigerated, must be used within 28 days after the first use. They must be discarded if not used within 28 days. If refrigeration is not possible, the open vial can be kept unrefrigerated for up to 28 days away from direct heat and light, as long as the temperature is not greater than 86°F (30°C).

Open (In-Use) Cartridge system:

The opened (in-use) cartridge system in OptiClik[®] should **NOT** be refrigerated but should be kept at room temperature (below 86°F [30°C]) away from direct heat and light. The opened (in-use) cartridge system in OptiClik[®] kept at room temperature must be discarded after 28 days. Do not store OptiClik[®], with or without cartridge system, in a refrigerator at any time.

Open (In-Use) SoloStar[®] disposable insulin device:

The opened (in-use) SoloStar[®] should **NOT** be refrigerated but should be kept at room temperature (below 86°F [30°C]) away from direct heat and light. The opened (in-use) SoloStar[®] kept at room temperature must be discarded after 28 days.

LANTUS should not be stored in the freezer and it should not be allowed to freeze. Discard if it has been frozen.

These storage conditions are summarized in the following table:

	Not in-use (unopened) Refrigerated	Not in-use (unopened) Room Temperature	In-use (opened) (See Temperature Below)
10 mL Vial	Until expiration date	28 days	28 days Refrigerated or room temperature
3 mL Cartridge system	Until expiration date	28 days	28 days Refrigerated or room temperature
3 mL Cartridge system inserted into OptiClik [®]			28 days Room temperature only (Do not refrigerate)
3 mL SoloStar [®] disposable insulin device	Until expiration date	28 days	28 days Room temperature only (Do not refrigerate)

Rev. March 2007

sanofi-aventis U.S. LLC
Bridgewater, NJ 08807

Country of Origin: Germany

www.lantus.com

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OptiClik[®] and SoloStar[®] are a registered trademark of sanofi-aventis U.S. LLC

‡ The brands listed are the trademarks of their respective owners and are not trademarks of sanofi-aventis U.S. LLC

Patient Information
LANTUS® SOLOSTAR® 3 mL disposable insulin delivery device (300 units per device)
100 units per mL (U-100)
(insulin glargine [recombinant DNA origin] injection)

- What is the most important information I should know about LANTUS?
- What is LANTUS?
- Who should NOT take LANTUS?
- How should I use LANTUS?
- Mixing with LANTUS
- Instructions for Use
- What can affect how much insulin I need?
- What are the possible side effects of LANTUS and other insulins?
- How should I store LANTUS?
- General Information about LANTUS

Read this “Patient Information” that comes with LANTUS (LAN-tus) before you start using it and each time you get a refill because there may be new information. This leaflet does not take the place of talking with your healthcare provider about your condition or treatment. If you have questions about LANTUS or about diabetes, talk with your healthcare provider.

What is the most important information I should know about LANTUS?

- **Do not change the insulin you are using without talking to your healthcare provider.** Any change of insulin should be made cautiously and only under medical supervision. Changes in insulin strength, manufacturer, type (for example: Regular, NPH, analogs), species (beef, pork, beef-pork, human) or method of manufacture (recombinant DNA versus animal-source insulin) may need a change in the dose. This dose change may be needed right away or later on during the first several weeks or months on the new insulin. Doses of oral anti-diabetic medicines may also need to change, if your insulin is changed.
- **You must test your blood sugar levels while using an insulin, such as LANTUS.** Your healthcare provider will tell you how often you should test your blood sugar level, and what to do if it is high or low.
- **Do NOT dilute or mix LANTUS with any other insulin or solution.** It will not work and you may lose blood sugar control, which could be serious.
- **LANTUS** comes as U-100 insulin and contains 100 units of LANTUS per milliliter (mL). One milliliter of U-100 insulin contains 100 units of insulin. (1 mL = 1 cc).

What is Diabetes?

- Your body needs insulin to turn sugar (glucose) into energy. If your body does not make enough insulin, you need to take more insulin so you will not have too much sugar in your blood.

- Insulin injections are important in keeping your diabetes under control. But the way you live, your diet, careful checking of your blood sugar levels, exercise, and planned physical activity, all work with your insulin to help you control your diabetes.

What is LANTUS?

- LANTUS (insulin glargine [recombinant DNA origin]) is a long-acting insulin. . Because Lantus is made by recombinant DNA technology (rDNA) and is chemically different from the insulin made by the human body, it is called an insulin analog. LANTUS is used to treat patients with diabetes for the control of high blood sugar. It is used once a day to lower blood glucose.
- LANTUS is a clear, colorless, sterile solution for injection under the skin (subcutaneously).
- The active ingredient in LANTUS is insulin glargine. The concentration of insulin glargine is 100 units per milliliter (mL), or U-100. LANTUS also contains zinc, metacresol, glycerol, and water for injection as inactive ingredients. Hydrochloric acid and/or sodium hydroxide may be added to adjust the pH.
- You need a prescription to get LANTUS. Always be sure you receive the right insulin from the pharmacy.

Who should NOT take LANTUS?

Do not take LANTUS if you are allergic to insulin glargine or any of the inactive ingredients in LANTUS. Check with your healthcare provider if you are not sure.

- **Before starting LANTUS, tell your healthcare provider about all your medical conditions including if you:**
 - **have liver or kidney problems.** Your dose may need to be adjusted.
 - **are pregnant or plan to become pregnant.** It is not known if LANTUS may harm your unborn baby. It is very important to maintain control of your blood sugar levels during pregnancy. Your healthcare provider will decide which insulin is best for you during your pregnancy.
 - **are breast-feeding or plan to breast-feed.** It is not known whether LANTUS passes into your milk. Many medicines, including insulin, pass into human milk, and could affect your baby. Talk to your healthcare provider about the best way to feed your baby.
 - **are taking any other medicines including** prescription and non-prescription medicines, vitamins and herbal supplements.

How should I use LANTUS?

See the "**Instructions for SoloStar[®] Use**" section for additional information.

- Follow the instructions given by your healthcare provider about the type or types of insulin you are using. Do not make any changes with your insulin unless you have talked to your healthcare provider. Your insulin needs may change because of illness, stress,

other medicines, or changes in diet or activity level. Talk to your healthcare provider about how to adjust your insulin dose.

- You may take LANTUS at any time during the day but you must take it at the same time every day.
- Only use LANTUS that is clear and colorless. If your LANTUS is cloudy or slightly colored, return it to your pharmacy for a replacement.
- Follow your healthcare provider's instructions for testing your blood sugar.
- Inject LANTUS under your skin (subcutaneously) in your upper arm, abdomen (stomach area), or thigh (upper leg). Never inject it into a vein or muscle.
- Change (rotate) injection sites within the same body area.
- **NEEDLES AND SOLOSTAR® MUST NOT BE SHARED.**
- Disposable needles should be used only once. Used needle should be placed in sharps containers (such as red biohazard containers), hard plastic containers (such as detergent bottles), or metal containers (such as an empty coffee can). Such containers should be sealed and disposed of properly.

Mixing with LANTUS

- **Do NOT dilute or mix LANTUS with any other insulin or solution.** It will not work as intended and you may lose blood sugar control, which could be serious.

Instructions for SoloStar® Use

It is important to read, understand, and follow the step-by-step instructions in the “SoloStar® Instruction Leaflet” before using SoloStar® disposable insulin Pen. Failure to follow the instructions may result in getting too much or too little insulin. If you have lost your leaflet or have a question, go to www.lantus.com or call 1-800-633-1610.

The following general notes should be taken into consideration before injecting Lantus:

- Always wash your hands before handling the SoloStar® disposable insulin Pen.
- Always attach a new needle before use. BD Ultra-Fine™ needles† are compatible with SoloStar. These are sold separately and are manufactured by BD.
- Always perform the safety test before use.
- Check the insulin solution in the pen to make sure it is clear, colorless, and free of particles. If it is not, throw it away.
- Do NOT mix or dilute LANTUS with any other insulin or solution. LANTUS will not work if it is mixed or diluted and you may lose blood sugar control, which could be serious.
- Decide on an injection area - either upper arm, thigh, or abdomen. Do not use the same injection site as your last injection.
- After injecting LANTUS, leave the needle in the skin for an additional 10 seconds. Then pull the needle straight out. Gently press on the spot where you injected yourself for a few seconds. **Do not rub the area.**
- Do not drop the SoloStar® disposable insulin Pen.

If your blood glucose reading is high or low, tell your healthcare provider so the dose can be adjusted.

What can affect how much insulin I need?

Illness. Illness may change how much insulin you need. It is a good idea to think ahead and make a "sick day" plan with your healthcare provider in advance so you will be ready when this happens. Be sure to test your blood sugar more often and call your healthcare provider if you are sick.

Medicines. Many medicines can affect your insulin needs. Other medicines, including prescription and non-prescription medicines, vitamins, and herbal supplements, can change the way insulin works. You may need a different dose of insulin when you are taking certain other medicines. **Know all the medicines you take**, including prescription and non-prescription medicines, vitamins and herbal supplements. You may want to keep a list of the medicines you take. You can show this list to your healthcare provider and pharmacists anytime you get a new medicine or refill. Your healthcare provider will tell you if your insulin dose needs to be changed.

Meals. The amount of food you eat can affect your insulin needs. If you eat less food, skip meals, or eat more food than usual, you may need a different dose of insulin. Talk to your healthcare provider if you change your diet so that you know how to adjust your LANTUS and other insulin doses.

Alcohol. Alcohol, including beer and wine, may affect the way LANTUS works and affect your blood sugar levels. Talk to your healthcare provider about drinking alcohol.

Exercise or Activity level. Exercise or activity level may change the way your body uses insulin. Check with your healthcare provider before you start an exercise program because your dose may need to be changed.

Travel. If you travel across time zones, talk with your healthcare provider about how to time your injections. When you travel, wear your medical alert identification. Take extra insulin and supplies with you.

Pregnancy or nursing. The effects of LANTUS on an unborn child or on a nursing baby are unknown. Therefore, tell your healthcare provider if you planning to have a baby, are pregnant, or nursing a baby. Good control of diabetes is especially important during pregnancy and nursing.

What are the possible side effects of LANTUS and other insulins?

Insulins, including LANTUS, can cause hypoglycemia (low blood sugar), hyperglycemia (high blood sugar), allergy, and skin reactions.

Hypoglycemia (low blood sugar):

Hypoglycemia is often called an "insulin reaction" or "low blood sugar". It may happen when you do not have enough sugar in your blood. Common causes of hypoglycemia are illness, emotional or physical stress, too much insulin, too little food or missed meals, and too much exercise or activity.

Early warning signs of hypoglycemia may be different, less noticeable or not noticeable at all in some people. That is why it is important to check your blood sugar as you have been advised by your healthcare provider.

Hypoglycemia can happen with:

- **Taking too much insulin.** This can happen when too much insulin is injected.
- **Not enough carbohydrate (sugar or starch) intake.** This can happen if a meal or snack is missed or delayed.
- **Vomiting or diarrhea** that decreases the amount of sugar absorbed by your body.
- **Intake of alcohol.**
- **Medicines that affect insulin.** Be sure to discuss all your medicines with your healthcare provider. **Do not start any new medicines until you know how they may affect your insulin dose.**
- **Medical conditions that can affect your blood sugar levels or insulin.** These conditions include diseases of the adrenal glands, the pituitary, the thyroid gland, the liver, and the kidney.
- **Too much glucose use by the body.** This can happen if you exercise too much or have a fever.
- **Injecting insulin the wrong way or in the wrong injection area.**

Hypoglycemia can be mild to severe. Its onset may be rapid. Some patients have few or no warning symptoms, including:

- patients with diabetes for a long time
- patients with diabetic neuropathy (nerve problems)
- or patients using certain medicines for high blood pressure or heart problems.

Hypoglycemia may reduce your ability to drive a car or use mechanical equipment and you may risk injury to yourself or others.

Severe hypoglycemia can be dangerous and can cause temporary or permanent harm to your heart or brain. **It may cause unconsciousness, seizures, or death.**

Symptoms of hypoglycemia may include:

- anxiety, irritability, restlessness, trouble concentrating, personality changes, mood changes, or other abnormal behavior
- tingling in your hands, feet, lips, or tongue

- dizziness, light-headedness, or drowsiness
- nightmares or trouble sleeping
- headache
- blurred vision
- slurred speech
- palpitations (fast heart beat)
- sweating
- tremor (shaking)
- unsteady gait (walking).

If you have hypoglycemia often or it is hard for you to know if you have the symptoms of hypoglycemia, talk to your healthcare provider.

Mild to moderate hypoglycemia is treated by eating or drinking carbohydrates such as fruit juice, raisins, sugar candies, milk or glucose tablets. Talk to your healthcare provider about the amount of carbohydrates you should eat to treat mild to moderate hypoglycemia.

Severe hypoglycemia may require the help of another person or emergency medical people. A person with hypoglycemia who is unable to take foods or liquids with sugar by mouth, or is unconscious needs medical help fast and will need treatment with a glucagon injection or glucose given intravenously (IV). Without medical help right away, serious reactions or even death could happen.

Hyperglycemia (high blood sugar):

Hyperglycemia happens when you have too much sugar in your blood. Usually, it means there is not enough insulin to break down the food you eat into energy your body can use. Hyperglycemia can be caused by a fever, an infection, stress, eating more than you should, taking less insulin than prescribed, or it can mean your diabetes is getting worse.

Hyperglycemia can happen with:

- **Insufficient (too little) insulin.** This can happen from:
 - injecting too little or no insulin
 - incorrect storage (freezing, excessive heat)
 - use after the expiration date.
- **Too much carbohydrate intake.** This can happen if you eat larger meals, eat more often, or increase the amount of carbohydrate in your meals.
- **Medicines that affect insulin.** Be sure to discuss all your medicines with your healthcare provider. **Do not start any new medicines until you know how they may affect your insulin dose.**
- **Medical conditions that affect insulin.** These medical conditions include fevers, infections, heart attacks, and stress.

- **Injecting insulin the wrong way or in the wrong injection area.**

Testing your blood or urine often will let you know if you have hyperglycemia. If your tests are often high, tell your healthcare provider so your dose of insulin can be changed.

Hyperglycemia can be mild or severe. It can **progress to diabetic ketoacidosis (DKA) or very high glucose levels (hyperosmolar coma) and result in unconsciousness and death.**

Although diabetic ketoacidosis occurs most often in patients with type 1 diabetes, it can also happen in patients with type 2 diabetes who become very sick. Because some patients get few symptoms of hyperglycemia, it is important to check your blood sugar/urine sugar and ketones regularly.

Symptoms of hyperglycemia include:

- confusion or drowsiness
- increased thirst
- decreased appetite, nausea, or vomiting
- rapid heart rate
- increased urination and dehydration (too little fluid in your body).

Symptoms of DKA also include:

- fruity smelling breath
- fast, deep breathing
- stomach area (abdominal) pain.

Severe or continuing hyperglycemia or DKA needs evaluation and treatment right away by your healthcare provider.

Do not use LANTUS to treat diabetic ketoacidosis.

Other possible side effects of LANTUS include:

Serious allergic reactions:

Some times severe, life-threatening allergic reactions can happen with insulin. If you think you are having a severe allergic reaction, get medical help right away. Signs of insulin allergy include:

- rash all over your body
- shortness of breath
- wheezing (trouble breathing)
- fast pulse
- sweating
- low blood pressure.

Reactions at the injection site:

Injecting insulin can cause the following reactions on the skin at the injection site:

- little depression in the skin (lipoatrophy)
- skin thickening (lipohypertrophy)
- red, swelling, itchy skin (injection site reaction).

You can reduce the chance of getting an injection site reaction if you change (rotate) the injection site each time. An injection site reaction should clear up in a few days or a few weeks. If injection site reactions do not go away or keep happening call your healthcare provider.

Tell your healthcare provider if you have any side effects that bother you.

These are not all the side effects of LANTUS. Ask your healthcare provider or pharmacist for more information.

How should I store LANTUS?

- **Unopened SoloStar®:**
Store new unopened SoloStar® disposable insulin pen in a refrigerator (not the freezer) between 36°F to 46°F (2°C to 8°C). Do not freeze LANTUS. Keep LANTUS out of direct heat and light. If a disposable insulin pen has been frozen or overheated, throw it away.
- **Open (In-Use) SoloStar®:**
Once SoloStar® is opened (in-use), SoloStar® should **NOT** be refrigerated but should be kept at room temperature (below 86°F [30°C]) away from direct heat and light. The opened (in-use) SoloStar® kept at room temperature must be discarded after 28 days.

These storage conditions are summarized in the following table:

	Not in-use (unopened) Refrigerated	Not in-use (unopened) Room Temperature	In-use (opened) Room Temperature (Do not refrigerate)
3 mL SoloStar® disposable insulin device	Until expiration date	28 days	28 days

- Do not use SoloStar® with LANTUS after the expiration date stamped on the label.
- Do not use LANTUS if it is cloudy, colored, or if you see particles.

General Information about LANTUS

- Use LANTUS only to treat your diabetes. **Do not** give or share LANTUS with another person, even if they have diabetes also. It may harm them.
- This leaflet summarizes the most important information about LANTUS. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about LANTUS that is written for healthcare professionals. For more information about LANTUS call 1-800-633-1610 or go to website www.lantus.com.

ADDITIONAL INFORMATION

DIABETES FORECAST is a national magazine designed especially for patients with diabetes and their families and is available by subscription from the American Diabetes Association (ADA), P.O. Box 363, Mt. Morris, IL 61054-0363, 1-800-DIABETES (1-800-342-2383). You may also visit the ADA website at www.diabetes.org.

Another publication, **COUNTDOWN**, is available from the Juvenile Diabetes Research Foundation International (JDRF), 120 Wall Street, 19th Floor, New York, New York 10005, 1-800-JDF-CURE (1-800-533-2873). You may also visit the JDRF website at www.jdf.org.

To get more information about diabetes, check with your healthcare professional or diabetes educator or visit www.DiabetesWatch.com.

Additional information about LANTUS can be obtained by calling 1-800-633-1610 or by visiting www.lantus.com.

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sanofi-aventis U.S. LLC
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LANTUS[®] SOLOSTAR[®]

(insulin glargine [rDNA origin] injection)

Instruction Leaflet

Your healthcare professional has decided that SoloStar[®] is right for you. Talk with your healthcare professional about proper injection technique before using SoloStar[®].

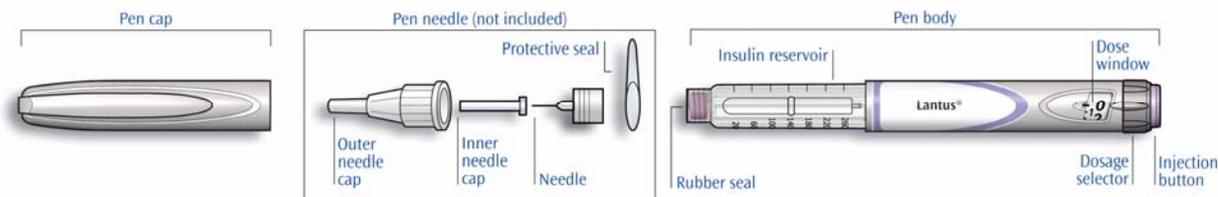
Read these instructions carefully before using your SoloStar[®]. If you are not able to follow all the instructions completely on your own, use SoloStar[®] only if you have help from a person who is able to follow the instructions.

Follow these instructions completely each time you use SoloStar[®] to ensure that you get an accurate dose. If you do not follow these instructions you may get too much or too little insulin, which may affect your blood glucose.

SoloStar[®] is a disposable pen for the injection of insulin. Each SoloStar[®] contains in total 300 units of insulin. You can set doses from 1 to 80 units in steps of 1 unit.

Keep this leaflet for future reference.

If you have any questions about SoloStar[®] or about diabetes, ask your healthcare professional, go to www.lantus.com or call sanofi aventis at 1-800-633-1610.



Important information for use of SoloStar[®]:

- Always attach a new needle before each use.
BD Ultra-Fine needles are compatible with SoloStar[®]. These are sold separately and are manufactured by BD. Contact your healthcare professional for further information.
- Always perform the safety test before each injection.
- This pen is only for your use. Do not share it with anyone else.
- If your injection is given by another person, special caution must be taken by this person to avoid accidental needle injury and transmission of infection.
- Never use SoloStar[®] if it is damaged or if you are not sure that it is working properly.
- Always have a spare SoloStar[®] in case your SoloStar[®] is lost or damaged.

Storage Instructions

Please check the leaflet for the insulin for complete instructions on how to store SoloStar[®].

If your SoloStar[®] is in cool storage, take it out 1 to 2 hours before you inject to allow it to warm up. Cold insulin is more painful to inject.

Keep SoloStar[®] out of the reach and sight of children.

Keep your SoloStar[®] in cool storage (36°F - 46°F [2°C – 8°C]) until first use. Do not allow it to freeze. Do not put it next to the freezer compartment of your refrigerator, or next to a freezer pack.

Once you take your SoloStar[®] out of cool storage, for use or as a spare, you can use it for up to 28 days. During this time it can be safely kept at room temperature up to 86°F (30°C). Do not use it after this time. SoloStar[®] in use must not be stored in a refrigerator.

Do not use SoloStar[®] after the expiration date printed on the label of the pen or on the carton.

Protect SoloStar[®] from light.

Discard your used SoloStar[®] as required by your local authorities.

Maintenance

Protect your SoloStar[®] from dust and dirt.

You can clean the outside of your SoloStar[®] by wiping it with a damp cloth.

Do not soak, wash or lubricate the pen as this may damage it.

Your SoloStar[®] is designed to work accurately and safely. It should be handled with care. Avoid situations where SoloStar[®] might be damaged. If you are concerned that your SoloStar[®] may be damaged, use a new one.

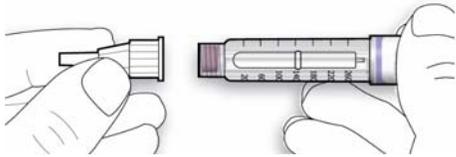
Step 1. Check the insulin

- A. Check the label on your SoloStar[®] to make sure you have the correct insulin.. The Lantus[®] SoloStar[®] is grey with a purple injection button.
- B. Take off the pen cap.
- C. Check the appearance of your insulin. Lantus[®] is a clear insulin. Do not use this SoloStar[®] if the insulin is cloudy, colored or has particles.

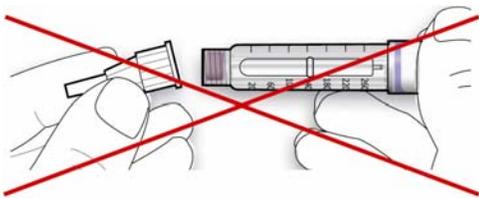
Step 2. Attach the needle

Always use a new sterile needle for each injection. This helps prevent contamination, and potential needle blocks.

- A. Wipe the Rubber Seal with alcohol.
- B. Remove the protective seal from a new needle.
- C. Line up the needle with the pen, and keep it straight as you attach it (screw or push on, depending on the needle type).



- If the needle is not kept straight while you attach it, it can damage the rubber seal and cause leakage, or break the needle.

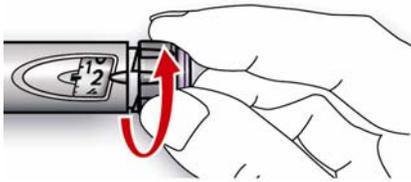


Step 3. Perform a Safety test

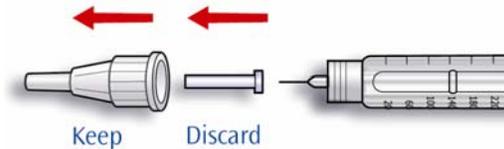
Always perform the safety test before each injection.

Performing the safety test ensures that you get an accurate dose by:

- ensuring that pen and needle work properly
 - removing air bubbles
- A. Select a dose of 2 units by turning the dosage selector.



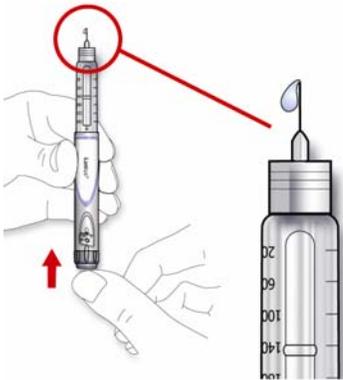
B. Take off the outer needle cap and keep it to remove the used needle after injection. Take off the inner needle cap and discard it.



C. Hold the pen with the needle pointing upwards.

D. Tap the insulin reservoir so that any air bubbles rise up towards the needle.

E. Press the injection button all the way in. Check if insulin comes out of the needle tip.



You may have to perform the safety test several times before insulin is seen.

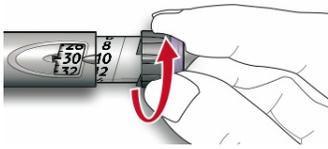
- If no insulin comes out, check for air bubbles and repeat the safety test two more times to remove them.
- If still no insulin comes out, the needle may be blocked. Change the needle and try again.
- If no insulin comes out after changing the needle, your SoloStar[®] may be damaged. Do not use this SoloStar[®].

Step 4. Select the dose

You can set the dose in steps of 1 unit, from a minimum of 1 unit to a maximum of 80 units. If you need a dose greater than 80 units, you should give it as two or more injections.

A. Check that the dose window shows “0” following the safety test.

B. Select your required dose (in the example below, the selected dose is 30 units). If you turn past your dose, you can turn back down.

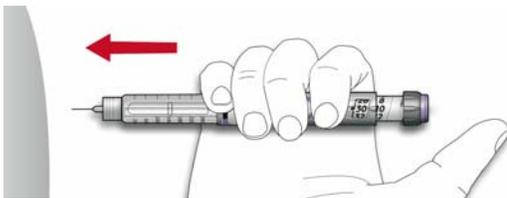


- Do not push the injection button while turning, as insulin will come out.
- You cannot turn the dosage selector past the number of units left in the pen. Do not force the dosage selector to turn. In this case, either you can inject what is remaining in the pen and complete your dose with a new SoloStar[®] or use a new SoloStar[®] for your full dose.

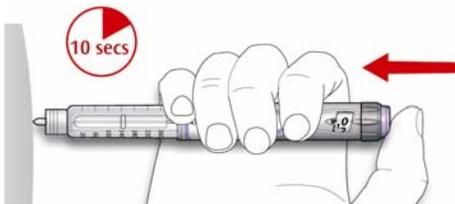
Step 5. Inject the dose

A. Use the injection method as instructed by your healthcare professional.

B. Insert the needle into the skin.



C. Deliver the dose by pressing the injection button in all the way. The number in the dose window will return to “0” as you inject.



D. Keep the injection button pressed all the way in.

Slowly count to 10 before you withdraw the needle from the skin. This ensures that the full dose will be delivered.

Step 6. Remove and discard the needle

Always remove the needle after each injection and store SoloStar without a needle attached. This helps prevent:

- Contamination and/or infection
- Entry of air into the insulin reservoir and leakage of insulin, which can cause inaccurate dosing.

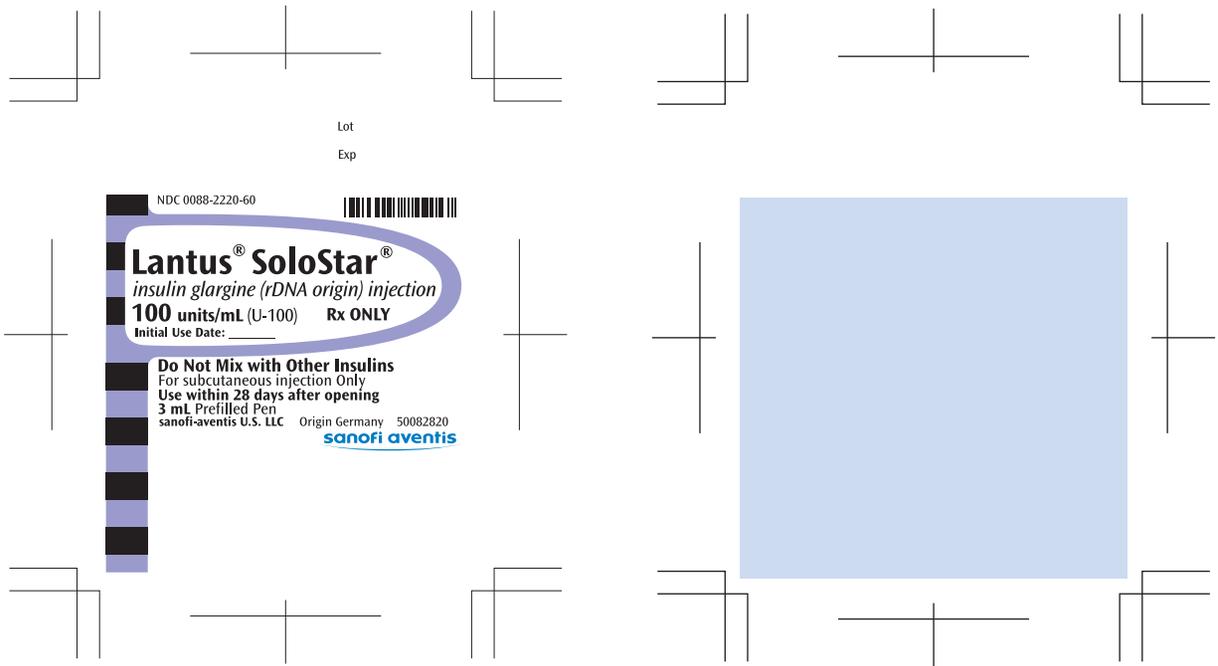
- A. Put the outer needle cap back on the needle, and use it to unscrew the needle from the pen. To reduce the risk of accidental needle injury, never replace the inner needle cap.
- If your injection is given by another person, special caution must be taken by this person when removing and disposing the needle. Follow recommended safety measures for removal and disposal of needles (e.g. a one handed capping technique) in order to reduce the risk of accidental needle injury and transmission of infectious diseases.
- B. Dispose of the needle safely. Used needles should be placed in sharps containers (such as red biohazard containers), hard plastic containers (such as detergent bottles), or metal containers (such as an empty coffee can). Such containers should be sealed and disposed of properly. If you are giving an injection to a third person, you should remove the needle in an approved manner to avoid needle-stick injuries.
- C. Always put the pen cap back on the pen, then store the pen until your next injection.

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Lot
Exp

NDC 0088-2220-60



Lantus[®] SoloStar[®]
insulin glargine (rDNA origin) injection
100 units/mL (U-100) Rx ONLY
Initial Use Date: _____

Do Not Mix with Other Insulins
For subcutaneous injection Only
Use within 28 days after opening
3 mL Prefilled Pen
sanofi-aventis U.S. LLC Origin Germany 50082820
sanofi aventis

