HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use LANTUS safely and effectively. See full prescribing information for LANTUS.

LANTUS® (insulin glargine injection) for subcutaneous injection

Initial U.S. Approval: 2000

INDICATIONS AND USAGE

LANTUS® is a long-acting human insulin analog indicated to improve glycemic control in adults and pediatric patients with type 1 diabetes mellitus and in adults with type 2 diabetes mellitus. (1)

DOSAGE FORMS AND STRENGTHS

Injection: 100 units/mL insulin glargine is available as:

- 10 mL multiple-dose vial (3)
- 3 mL single-patient-use SoloStar prefilled pen (3)

CONTRAINDICATIONS

- Hypersensitivity to LANTUS or one of its excipients (4)

ADVERSE REACTIONS

- Hypoglycemia (4)
- Edema (6.1)
- Weight gain (6.1)

WARNINGS AND PRECAUTIONS

- Never share a LANTUS SoloStar prefilled pen between patients, even if the needle is changed. (5.1)
- Hypoglycemia or hypoglycemia with changes in insulin regimen: Carrying out under close medical supervision. (5.2)
- Hypoglycemia: May be life-threatening. Increase frequency of glucose monitoring with changes to: insulin dosage, coadministered glucose lowering medications, meal pattern, physical activity; and in patients with renal or hepatic impairment and hypoglycemia unawareness. (5.3, 6.1)
- Medication Errors: Accidental mix-ups between insulin products can occur. Instruct patients to check insulin labels before injection. (5.4, 6.3)
- Hypersensitivity reactions: Severe, life-threatening, generalized allergy, including anaphylaxis, can occur. Discontinue LANTUS. Monitor and treat if indicated. (5.5, 6.1)
- Hypokalemia: May be life-threatening. Monitor potassium levels in patients at risk of hypokalemia and treat if indicated. (5.6)
- Fluid retention and heart failure with concomitant use of thiazolidinediones (TZDs): Observe for signs and symptoms of heart failure; consider dosage reduction or discontinuation of TZD if heart failure occurs. (5.7)

DRUG INTERACTIONS

- Drugs that affect glucose metabolism: Adjustment of insulin dosage may be needed; closely monitor of blood glucose. (7)
- Antidiabetic Drugs (e.g., beta-blockers, clonidine, guanethidine, and reserpine): Signs and symptoms of hypoglycemia may be reduced or absent. (7)

INFORMATION FOR PATIENTS

- Use during pregnancy only if the potential benefit justifies the potential risk to the fetus. (8.1)

HOW SUPPLIED/STORAGE AND HANDLING

Sanofi-aventis at 1-800-633-1610 or www.fda.gov/medwatch.

PATIENT COUNSELING INFORMATION

- Use during pregnancy only if the potential benefit justifies the potential risk to the fetus. (8.1)
LANTUS is contraindicated in patients who have had hypersensitivity reactions to insulin glargine or one of the excipients who experience recurrent hypoglycemia.

5.4 Medication Errors

The following adverse reactions are discussed elsewhere:

- Hypoglycemia [see Warnings and Precautions (5.3)]
- Hypersensitivity and allergic reactions [see Warnings and Precautions (5.5)]

5.6 Hypokalemia

Hypoglycemia in patients with type 1 diabetes mellitus and type 2 diabetes mellitus are listed in the tables below.

### Table 1: Adverse Events in Pooled Clinical Trials up to 28 Weeks Duration in Adults with Type 1 Diabetes (adverse events with frequency ≥5%)

<table>
<thead>
<tr>
<th>Condition</th>
<th>LANTUS, % (n=1257)</th>
<th>NPH, % (n=1070)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoglycemia</td>
<td>22.4</td>
<td>23.1</td>
</tr>
<tr>
<td>Injection*</td>
<td>9.4</td>
<td>10.3</td>
</tr>
<tr>
<td>Accidental injury</td>
<td>5.7</td>
<td>6.4</td>
</tr>
<tr>
<td>Headache</td>
<td>5.5</td>
<td>4.7</td>
</tr>
</tbody>
</table>

*Body system not specified

### Table 2: Adverse Events in Pooled Clinical Trials up to 1 Year Duration in Adults with Type 2 Diabetes (adverse events with frequency ≥5%)

<table>
<thead>
<tr>
<th>Condition</th>
<th>LANTUS, % (n=849)</th>
<th>NPH, % (n=714)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper respiratory tract infection</td>
<td>11.4</td>
<td>13.3</td>
</tr>
<tr>
<td>Injection*</td>
<td>10.4</td>
<td>11.6</td>
</tr>
<tr>
<td>Retinal vascular disorder</td>
<td>5.8</td>
<td>7.4</td>
</tr>
</tbody>
</table>

*Body system not specified

### Table 3: Adverse Events in a 5-Year Trial of Adults with Type 2 Diabetes (adverse events with frequency ≥10%)

<table>
<thead>
<tr>
<th>Condition</th>
<th>LANTUS, % (n=514)</th>
<th>NPH, % (n=503)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper respiratory tract infection</td>
<td>20.7</td>
<td>30.6</td>
</tr>
<tr>
<td>Edema peripheral</td>
<td>29.0</td>
<td>25.0</td>
</tr>
<tr>
<td>Hypertension</td>
<td>19.5</td>
<td>18.9</td>
</tr>
<tr>
<td>Fluorescein retinal breakage</td>
<td>18.7</td>
<td>19.5</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>18.0</td>
<td>17.9</td>
</tr>
<tr>
<td>Cataract</td>
<td>17.4</td>
<td>15.9</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>14.5</td>
<td>14.1</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>14.2</td>
<td>16.1</td>
</tr>
<tr>
<td>Pain in extremity</td>
<td>13.1</td>
<td>13.1</td>
</tr>
<tr>
<td>Back pain</td>
<td>12.8</td>
<td>12.3</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>12.5</td>
<td>10.7</td>
</tr>
</tbody>
</table>

*Body system not specified
**Severe Hypoglycemia**

Table 7 displays the proportion of patients experiencing severe symptomatic hypoglycemia in the two treatment groups compared to the adult trials with type 1 diabetes.

<table>
<thead>
<tr>
<th></th>
<th>LANTUS, % (n=292)</th>
<th>NPH, % (n=293)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>10.5</td>
<td>9.7</td>
</tr>
<tr>
<td>Headache</td>
<td>10.3</td>
<td>9.3</td>
</tr>
</tbody>
</table>

*Body system not specified*

Severe Hypoglycemia

Hypoglycemia is the most commonly observed adverse reaction in patients using insulin, including LANTUS [see Warnings and Precautions (5.3)]. Tables 5, 6 and 7 summarize the incidence of severe hypoglycemia in the LANTUS individual clinical trials. Severe symptomatic hypoglycemia was defined as an event with symptoms consistent with hypoglycemia requiring the assistance of another person and associated with either a blood glucose below 50 mg/dL (≤25 mmol/L) in the 5-year trial and ≤36 mg/dL (≤2.0 mmol/L) in the ORIGIN trial or prompt recovery after oral carbohydrate, intravenous glucose or glucagon administration.

Percentages of LANTUS-treated adult patients experiencing severe symptomatic hypoglycemia in the LANTUS clinical trials [see Clinical Studies (14)] were comparable to percentages of NPH-treated patients for all treatment regimens [see Tables 5 and 6]. In the pediatric phase 3 clinical trial, children and adolescents with type 1 diabetes had a higher incidence of severe symptomatic hypoglycemia in the two treatment groups compared to the adult trial with type 1 diabetes.

Table 5: Severe Symptomatic Hypoglycemia in Patients with Type 1 Diabetes

<table>
<thead>
<tr>
<th></th>
<th>Study A</th>
<th>Study B</th>
<th>Study C</th>
<th>Study D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1 Diabetes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults 28 weeks</td>
<td>LANTUS</td>
<td>NPH</td>
<td>LANTUS</td>
<td>LANTUS</td>
</tr>
<tr>
<td>In combination</td>
<td>N=292</td>
<td>N=293</td>
<td>N=264</td>
<td>N=270</td>
</tr>
<tr>
<td>with regular</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>insulin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent of</td>
<td>10.6</td>
<td>15.0</td>
<td>8.7</td>
<td>6.6</td>
</tr>
<tr>
<td>patients</td>
<td></td>
<td></td>
<td></td>
<td>5.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>23.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>28.6</td>
</tr>
</tbody>
</table>

**Peripheral Edema**

Some patients taking LANTUS have experienced sodium retention and edema, particularly if previously poor metabolic control is improved by intensified insulin therapy.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There are no well-controlled clinical studies of the use of LANTUS in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. All pregnancies have a background risk of birth defects, loss, or other adverse outcome regardless of drug exposure. This background risk is increased in pregnancies complicated by hyperglycemia and may be decreased with good metabolic control. It is essential for patients with diabetes or gestational diabetes to maintain good metabolic control before conception and throughout pregnancy. In patients with diabetes or gestational diabetes, insulin requirements may decrease during the first trimester, generally increase during the second trimester, and rapidly decline after delivery. Careful monitoring of glucose control is essential in these patients. Therefore, female patients should be advised to tell their physicians if they intend to become, or if they become pregnant while taking LANTUS.

8.2 Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. All insulin products can elicit the formation of insulin antibodies. The presence of such insulin antibodies may increase or decrease the efficacy of insulin and may require adjustment of the insulin dose. In phase 3 clinical trials of LANTUS, increases in titers of antibodies to insulin were observed in NPH insulin and LANTUS treatment groups with similar incidences.

8.3 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of LANTUS. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. Medication errors have been reported in which other insulins, particularly rapid-acting insulins, have been accidentally administered instead of LANTUS [see Patient Counseling Information (17)]. To avoid medication errors between LANTUS and other insulins, patients should be instructed to always verify the insulin label before each injection.

7 DRUG INTERACTIONS

Table 8 shows clinically significant drug interactions with LANTUS.
Subcutaneous reproduction and teratology studies have been performed with insulin glargine and regular human insulin in rabbits and rats. Insulin glargine 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 Units/day (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 Units/day (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.

8.3 Nursing Mothers
Endogenous insulin is present in human milk; it is unknown whether insulin glargine is excreted in human milk. Because many drugs, including human insulin, are excreted in human milk, caution should be exercised when LANTUS is administered to a nursing woman. Use of LANTUS is compatible with breastfeeding, but women with diabetes who are lactating may require adjustments of their insulin doses.

8.4 Pediatric Use
The safety and effectiveness of LANTUS have been established in pediatric patients (age 6 to 15 years) with type 1 and type 2 diabetes [see Clinical Studies (14)]. LANTUS consists of insulin glargine dissolved in a clear aqueous fluid. Each milliliter of LANTUS contains the following inactive ingredients per mL: 30 mcg zinc, 2.7 mg m-cresol, 20 mg glycerol 85%, 20 mcg polysorbate 20, 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.

12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
The primary activity of insulin, including insulin glargine, is regulation of glucose metabolism. Insulin and its analogs lower blood glucose by stimulating peripheral glucose uptake, especially by skeletal muscle and fat, and by inhibiting hepatic glucose production. Insulin inhibits lipolysis and proteolysis, and enhances protein synthesis.

12.2 Pharmacodynamics
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 that for human insulin. Figure 1 shows the time course of action 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 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

The 3 mL prefilled pen presentation contains the following inactive ingredients per mL: 30 mcg zinc, 2.7 mg m-cresol, 20 mg glycerol 85%, 20 mcg polysorbate 20, and water for injection. **The duration of action after abdominal, deltoid, or thigh subcutaneous administration was similar.** The time course of action of insulins, including LANTUS, may vary between individuals and within the same individual.

12.3 Pharmacokinetics
Absorption and Bioavailability
After subcutaneous injection of LANTUS 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 insulin. Metabolism and Elimination
A pharmacokinetic 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 human insulin, M1 (21'-Gly-insulin) and M2 (21'-Gly-des-30-Thr-insulin). Unchanged drug and these degradation products are also present in the circulation.

14 CLINICAL STUDIES
14.1 Overview of Clinical Studies
The safety and effectiveness of LANTUS given once-daily at bedtime was compared to that of once-daily and twice-daily NPH insulin in open-label, randomized, active-controlled, parallel studies of 2,327 adult patients and 349 pediatric patients with type 1 diabetes mellitus and 1,563 adult patients with type 2 diabetes mellitus (see Tables 9–11). In general, the reduction in glycated hemoglobin (HbA1c) with LANTUS was similar to that with NPH insulin.

14.2 Clinical Studies in Adult and Pediatric Patients with Type 1 Diabetes
In two clinical studies (Studies A and B), patients with type 1 diabetes (Study A: n=585, Study B: n=534) were randomized to 26 weeks of basal-bolus treatment with LANTUS or NPH insulin. Regular human
insulin was administered before each meal. LANTUS was administered at bedtime, NPH insulin was administered either as once daily at bedtime or in the morning and at bedtime when used twice daily. In Study A, the average age was 39.2 years. The majority of patients were White (99%) and 53.7% were male. The mean BMI was approximately 24.9 kg/m². The mean duration of diabetes was 15.5 years.

In Study B, the average age was 38.5 years. The majority of patients were White (95.3%) and 50.6% were male. The mean BMI was approximately 25.8 kg/m². The mean duration of diabetes was 17.4 years.

In another clinical study (Study C), patients with type 1 diabetes (n=619) were randomized to 16 weeks of basal-bolus treatment with LANTUS or NPH insulin. Insulin lispro was used before each meal. LANTUS was administered once daily at bedtime and NPH insulin was administered once or twice daily. The average age was 39.2 years. The majority of patients were White (96.9%) and 50.6% were male. The mean BMI was approximately 25.6 kg/m². The mean duration of diabetes was 18.5 years.

In these 3 studies, LANTUS and NPH insulin had similar effects on HbA1c (Table 9) with a similar overall rate of severe symptomatic hypoglycemia [see Adverse Reactions (6.1)].

### Table 9: Type 1 Diabetes Mellitus – Adult

<table>
<thead>
<tr>
<th>Treatment duration</th>
<th>Study A</th>
<th>Study B</th>
<th>Study C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment in combination with</td>
<td>28 weeks</td>
<td>28 weeks</td>
<td>16 weeks</td>
</tr>
<tr>
<td>Number of subjects treated</td>
<td>292</td>
<td>293</td>
<td>264</td>
</tr>
<tr>
<td>HbA1c</td>
<td>Baseline</td>
<td>Baseline</td>
<td>Baseline</td>
</tr>
<tr>
<td>Adj. mean change at trial end</td>
<td>0.2</td>
<td>0.1</td>
<td>-0.2</td>
</tr>
<tr>
<td>Treatment Difference (95% CI)</td>
<td>+0.1 (-0.2; +0.2)</td>
<td>+0.1 (-0.1; +0.2)</td>
<td>0.0 (-0.1; +0.1)</td>
</tr>
<tr>
<td>Basal insulin dose</td>
<td>Baseline</td>
<td>Baseline</td>
<td>Baseline</td>
</tr>
<tr>
<td>Mean change from baseline</td>
<td>-2</td>
<td>0</td>
<td>-4</td>
</tr>
<tr>
<td>Total insulin dose</td>
<td>Baseline</td>
<td>Baseline</td>
<td>Baseline</td>
</tr>
<tr>
<td>Mean change from baseline</td>
<td>-1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Fasting blood glucose (mg/dL)</td>
<td>Baseline</td>
<td>Baseline</td>
<td>Baseline</td>
</tr>
<tr>
<td>Adj. mean change from baseline</td>
<td>-21</td>
<td>-16</td>
<td>-20</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>Baseline</td>
<td>Baseline</td>
<td>Baseline</td>
</tr>
<tr>
<td>Mean change from baseline</td>
<td>73.2</td>
<td>74.8</td>
<td>75.5</td>
</tr>
<tr>
<td>Mean change from baseline</td>
<td>0.1</td>
<td>-0.0</td>
<td>0.7</td>
</tr>
</tbody>
</table>

Type 1 Diabetes – Pediatric (see Table 10)

In a randomized, controlled clinical study (Study D) (n=570), LANTUS was evaluated for 52 weeks in combination with oral antidiabetic medications (a sulfonylurea, metformin, acarbose, or combinations of these drugs). The average age was 59.5 years. The majority of patients were White (92.8%) and 53% were male. The mean BMI was approximately 29.1 kg/m². The mean duration of diabetes was 10.8 years. LANTUS was administered once daily at bedtime and NPH insulin administered once daily at bedtime in reducing HbA1c and fasting glucose (Table 11). The rate of severe symptomatic hypoglycemia was similar in LANTUS and NPH insulin treated patients [see Adverse Reactions (6.1)].

In a randomized, controlled clinical study (Study F), in patients with type 2 diabetes not using oral antidiabetic medications (n=518), a basal-bolus regimen of LANTUS once daily at bedtime or NPH insulin administered once or twice daily was evaluated for 28 weeks. Regular human insulin was used before meals, as needed. The average age was 59.5 years. The majority of patients were White (80.7%) and 60% were male. The mean BMI was approximately 30.5 kg/m². The mean duration of diabetes was 13.7 years. LANTUS had similar effectiveness as either once- or twice-daily NPH insulin in reducing HbA1c and fasting glucose (Table 11) with a similar incidence of hypoglycemia [see Adverse Reactions (6.1)].

In a randomized, controlled clinical study (Study G), patients with type 2 diabetes were randomized to 5 years of treatment with once-daily LANTUS or twice-daily NPH insulin. For patients not previously treated with insulin, the starting dose of LANTUS or NPH insulin was 10 units daily. Patients who were already treated with NPH insulin either continued on the same total daily NPH insulin dose or started LANTUS at a dose that was 80% of the total previous NPH insulin dose. The primary endpoint for this study was a comparison of the progression of diabetic retinopathy by 3 or more steps on the Early Treatment Diabetic Retinopathy Study (ETDRS) scale. HbA1c change from baseline was a secondary endpoint. Similar glycemic control in the 2 treatment groups was desired in order to not confound the interpretation of the retinal data. Patients or study personnel used an algorithm to adjust the LANTUS and NPH insulin doses to a target fasting plasma glucose ≤100 mg/dL. After the LANTUS or NPH insulin dose was adjusted, other antidiabetic agents, including pre-meal insulin were to be adjusted or added. The average age was 55.1 years. The majority of patients were White (85.3%) and 53% were male. The mean BMI was approximately 34.3 kg/m². The mean duration of diabetes was 10.8 years. The LANTUS group had a smaller mean reduction from baseline in HbA1c compared to the NPH insulin group, which may be explained by the lower daily basal insulin doses in the LANTUS group (Table 11). The incidences of severe symptomatic hypoglycemia were similar between groups [see Adverse Reactions (6.1)].

### Table 10: Type 1 Diabetes Mellitus – Pediatric

<table>
<thead>
<tr>
<th>Treatment duration</th>
<th>Study D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment in combination with</td>
<td>28 weeks</td>
</tr>
<tr>
<td>Number of subjects treated</td>
<td>269</td>
</tr>
<tr>
<td>HbA1c</td>
<td>Baseline</td>
</tr>
<tr>
<td>Baseline mean</td>
<td>8.5</td>
</tr>
<tr>
<td>Adjusted mean change from baseline</td>
<td>-0.5</td>
</tr>
<tr>
<td>Mean change from baseline</td>
<td>-0.5</td>
</tr>
<tr>
<td>(95% CI for Treatment difference)</td>
<td>(-0.3; +0.1)</td>
</tr>
</tbody>
</table>

### Table 11: Type 2 Diabetes Mellitus – Adult

<table>
<thead>
<tr>
<th>Treatment duration</th>
<th>Study E</th>
<th>Study F</th>
<th>Study G</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment in combination with</td>
<td>52 weeks</td>
<td>28 weeks</td>
<td>5 years</td>
</tr>
<tr>
<td>Number of subjects treated</td>
<td>289</td>
<td>261</td>
<td>513</td>
</tr>
<tr>
<td>HbA1c</td>
<td>Baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline mean</td>
<td>8.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted mean change from baseline</td>
<td>-0.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean change from baseline</td>
<td>-0.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(95% CI for Treatment difference)</td>
<td>(-0.3; +0.1)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 10: Type 1 Diabetes Mellitus – Pediatric (continued)

<table>
<thead>
<tr>
<th>Treatment duration</th>
<th>Study D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment in combination with</td>
<td>28 weeks</td>
</tr>
<tr>
<td>Number of subjects treated</td>
<td>289</td>
</tr>
<tr>
<td>HbA1c</td>
<td>Baseline</td>
</tr>
<tr>
<td>Baseline mean</td>
<td>8.9</td>
</tr>
<tr>
<td>Adjusted mean change from baseline</td>
<td>-0.5</td>
</tr>
<tr>
<td>Mean change from baseline</td>
<td>-0.5</td>
</tr>
<tr>
<td>(95% CI for Treatment difference)</td>
<td>(-0.3; +0.1)</td>
</tr>
</tbody>
</table>

### Table 11: Type 2 Diabetes Mellitus – Adult

<table>
<thead>
<tr>
<th>Treatment duration</th>
<th>Study E</th>
<th>Study F</th>
<th>Study G</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment in combination with</td>
<td>52 weeks</td>
<td>28 weeks</td>
<td>5 years</td>
</tr>
<tr>
<td>Number of subjects treated</td>
<td>269</td>
<td>261</td>
<td>513</td>
</tr>
<tr>
<td>HbA1c</td>
<td>Baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline mean</td>
<td>8.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted mean change from baseline</td>
<td>-0.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean change from baseline</td>
<td>-0.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(95% CI for Treatment difference)</td>
<td>(-0.3; +0.1)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 11: Type 2 Diabetes Mellitus – Adult (continued)

Treatment duration
<table>
<thead>
<tr>
<th>Treatment in combination with</th>
<th>Treatment in combination with</th>
<th>Study E 52 weeks Oral agents</th>
<th>Study F 28 weeks Regular insulin</th>
<th>Study G 5 years Regular insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal insulin dose*</td>
<td>Basal insulin dose*</td>
<td>LANTUS (%) NPH (%) Difference*</td>
<td>LANTUS (%) NPH (%) Difference*</td>
<td></td>
</tr>
<tr>
<td>Baseline mean</td>
<td>14</td>
<td>15</td>
<td>44.1</td>
<td>45.5</td>
</tr>
<tr>
<td>Mean change from baseline</td>
<td>+12</td>
<td>+9</td>
<td>-1</td>
<td>-7</td>
</tr>
<tr>
<td>Total insulin dose</td>
<td>Baseline mean</td>
<td>14</td>
<td>15</td>
<td>64</td>
</tr>
<tr>
<td>Mean change from baseline</td>
<td>+12</td>
<td>+9</td>
<td>+10</td>
<td>+13</td>
</tr>
<tr>
<td>Fasting blood glucose (mg/dL)</td>
<td>Baseline mean</td>
<td>78.5</td>
<td>82.1</td>
<td>89.6</td>
</tr>
<tr>
<td>Mean change from baseline</td>
<td>-49</td>
<td>-46</td>
<td>-24</td>
<td>-22</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>Baseline mean</td>
<td>83.5</td>
<td>82.1</td>
<td>89.6</td>
</tr>
<tr>
<td>Mean change from baseline</td>
<td>2.0</td>
<td>1.9</td>
<td>0.4</td>
<td>1.4</td>
</tr>
</tbody>
</table>

*In Study G, the baseline dose of basal or total insulin was the first available on-treatment dose prescribed during the study (on visit month 1.5).

LANTUS Timing of Daily Dosing (see Table 12)

The safety and efficacy of LANTUS administered pre-breakfast, pre-dinner, or at bedtime were evaluated in a randomized, controlled clinical study in patients with type 1 diabetes (study H, n=378). Patients were also treated with insulin lispro at mealtime. The average age was 40.9 years. All patients were White (100%) and 53.7% were male. The mean BMI was approximately 25.3 kg/m². The mean duration of diabetes was 17.3 years. LANTUS administered at different times of the day resulted in similar reductions in HbA1c compared to that with bedtime administration (see Table 12). In these patients, data are available from 8-point home glucose monitoring. The maximum mean blood glucose was observed just prior to injection of LANTUS regardless of time of administration.

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. The safety and efficacy of LANTUS administered pre-breakfast or at bedtime were also evaluated in a randomized, active-controlled clinical study (Study I, n=697) in patients with type 2 diabetes not adequately controlled on oral antidiabetic therapy. All patients in this study also received glimepiride 3 mg daily. The average age was 60.8 years. The majority of patients were White (96.6%) and 53.7% were male. The mean BMI was approximately 28.7 kg/m². The mean duration of diabetes was 10.1 years. LANTUS given before breakfast was at least as effective in lowering HbA1c as LANTUS given at bedtime or NPH insulin given at bedtime (see Table 12).

Table 12: LANTUS Timing of Daily Dosing in Type 1 (Study H) and Type 2 (Study I) Diabetes Mellitus

<table>
<thead>
<tr>
<th>Treatment duration</th>
<th>Treatment in combination with</th>
<th>Study H 24 weeks Insulin lispro</th>
<th>Study I 24 weeks Glimepiride</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal insulin dose (U)</td>
<td>Baseline mean</td>
<td>22</td>
<td>23</td>
</tr>
<tr>
<td>Mean change from baseline</td>
<td>5</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Total insulin dose (U)</td>
<td>Baseline mean</td>
<td>52</td>
<td>52</td>
</tr>
</tbody>
</table>

Five-Year Trial Evaluating the Progression of Retinopathy

Retinopathy was evaluated in the LANTUS clinical studies by analysis of reported retinal adverse events and fundus photography. The numbers of retinal adverse events reported for LANTUS and NPH insulin treatment groups were similar for patients with type 1 and type 2 diabetes. LANTUS was compared to NPH insulin in a 5-year randomized clinical trial that evaluated the progression of retinopathy as assessed with fundus photography using a grading protocol derived from the Early Treatment Diabetic Retinopathy Scale (ETDRS). Patients had type 2 diabetes (mean age 55 yrs) with no (86%) or mild (14%) retinopathy at baseline. Mean baseline HbA1c was 8.4%. The primary outcome was progression by 3 or more steps on the ETDRS scale at study endpoint. Patients with prespecified postbaseline eye procedures (pan-retinal photocoagulation for proliferative or severe nonproliferative diabetic retinopathy, local photocoagulation for new vessels, and vitrectomy for diabetic retinopathy) were also considered as 3-step progressors regardless of actual change in ETDRS score from baseline. Retinopathy graders were blinded to treatment group assignment. The results for the primary endpoint are shown in Table 13 for both the per-protocol and Intent-to-Treat populations, and indicate similarity of LANTUS to NPH in the progression of diabetic retinopathy as assessed by this outcome.

Table 13: Number (%) of Patients with 3 or More Step Progression on ETDRS Scale at Endpoint

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>LANTUS (%)</th>
<th>NPH (%)</th>
<th>Difference* (SE)</th>
<th>95% CI for difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Per-protocol</td>
<td>53/374 (14.2%)</td>
<td>57/363 (15.7%)</td>
<td>-2.0% (2.6%)</td>
<td>-7.0% to +3.1%</td>
</tr>
<tr>
<td>Intent-to-Treat</td>
<td>63/502 (12.5%)</td>
<td>71/487 (14.6%)</td>
<td>-2.1% (2.1%)</td>
<td>-6.3% to +2.1%</td>
</tr>
</tbody>
</table>

*Difference = LANTUS – NPH
† Using a generalized linear model (SAS GENMOD) with treatment and baseline HbA1c strata (cutoff 9.0%) as the classified independent variables, and with binomial distribution and identity link function

The Origin Study

The Outcome Reduction with Initial Glargine Intervention trial (i.e., ORIGIN) was an open-label, randomized, 2-by-2, factorial design study. One intervention in ORIGIN compared the effect of LANTUS to standard care on major adverse cardiovascular outcomes in 12,537 participants ≥50 years of age with abnormal glucose levels (i.e., impaired fasting glucose [IFG] and/or impaired glucose tolerance [IGT]) or early type 2 diabetes mellitus and established cardiovascular (i.e., CV disease or CV risk factors) at baseline.

The objective of the trial was to demonstrate that LANTUS use could significantly lower the risk of major cardiovascular outcomes compared to standard care. Two coprimary composite cardiovascular endpoints were used in ORIGIN. The first coprimary endpoint was the time to first occurrence of a major adverse cardiovascular event defined as the composite of CV death, nonfatal myocardial infarction and nonfatal stroke. The second coprimary endpoint was the time to the first occurrence of CV death or nonfatal myocardial infarction or nonfatal stroke or revascularization procedure or hospitalization for heart failure.

Participants were randomized to either LANTUS (N=6284) titrated to a target fasting plasma glucose of ≤95 mg/dL or to standard care (N=6273). Anthropometric and disease characteristics were balanced at baseline. The mean age was 64 years and 8% of participants were 75 years of age or older. The majority of participants were male (65%). Fifty nine percent were Caucasian, 25% were Latin, 10% were Asian and 9% were Black. The median baseline BMI was 29 kg/m². Approximately 12% of participants had abnormal glucose levels (IGT and/or IFG) at baseline and 88% had type 2 diabetes. For patients with type 2 diabetes, 59% were treated with a single oral antidiabetic drug, 23% had known diabetes but were on no antidiabetic drug and 6% were newly diagnosed during the screening procedure. The mean HbA1c (SD) at baseline was 6.5% (1.0). Fifty-nine percent of participants had a prior cardiovascular event and 39% had documented coronary artery disease or other cardiovascular risk factors.

Vital status was available for 99.9% and 99.8% of participants randomized to LANTUS and standard care respectively at end of trial. The median duration of follow-up was 6.2 years (range: 8 days to 7.9 years). The mean HbA1c (SD) at the end of the trial was 6.5% (1.1) and 6.8% (1.2) in the LANTUS and standard care group respectively. The median dose of LANTUS at end of trial was 0.45 U/kg. Eighty-one percent of patients randomized to LANTUS were using LANTUS at end of the study. The mean change in body weight from baseline to the last treatment visit was 2.2 kg greater in the LANTUS group than in the standard care group.

Overall, the incidence of major adverse cardiovascular outcomes was similar between groups (see Table 14). All-cause mortality was also similar between groups.
In the ORIGIN trial, the overall incidence of cancer (all types combined) or death from cancer (Table 1) was similar between treatment groups.

Table 14: Cardiovascular Outcomes in ORIGIN - Time to First Event Analyses

<table>
<thead>
<tr>
<th>COPRIMARY ENDPOINTS</th>
<th>LANTUS N=6264</th>
<th>Standard Care N=6273</th>
<th>LANTUS vs Standard Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV death, nonfatal myocardial infarction, or nonfatal stroke</td>
<td>1041 (2.9)</td>
<td>1013 (2.9)</td>
<td>1.02 (0.94, 1.11)</td>
</tr>
<tr>
<td>CV death, nonfatal myocardial infarction, nonfatal stroke, hospitalization for heart failure or revascularization procedure</td>
<td>1792 (5.5)</td>
<td>1727 (5.3)</td>
<td>1.04 (0.97, 1.11)</td>
</tr>
</tbody>
</table>

Components of coprimary endpoints

| CV death | 580 | 576 | 1.00 (0.89, 1.13) |
| Myocardial Infarction (fatal or non-fatal) | 336 | 326 | 1.03 (0.88, 1.19) |
| Stroke (fatal or non-fatal) | 331 | 319 | 1.03 (0.89, 1.21) |
| Revascularizations | 908 | 860 | 1.06 (0.95, 1.16) |
| Hospitalization for heart failure | 310 | 343 | 0.90 (0.77, 1.05) |

In the ORIGIN trial, the overall incidence of cancer (all types combined) or death from cancer (Table 15) was similar between treatment groups.

Table 15: Cancer Outcomes in ORIGIN – Time to First Event Analyses

<table>
<thead>
<tr>
<th>CANCER ENDPOINTS</th>
<th>LANTUS N=6264</th>
<th>Standard Care N=6273</th>
<th>LANTUS vs Standard Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any cancer event (new or recurrent)</td>
<td>559 (1.56)</td>
<td>551 (1.56)</td>
<td>0.99 (0.88, 1.11)</td>
</tr>
<tr>
<td>New cancer events</td>
<td>524 (1.46)</td>
<td>535 (1.49)</td>
<td>0.96 (0.85, 1.09)</td>
</tr>
<tr>
<td>Death due to Cancer</td>
<td>189 (0.51)</td>
<td>201 (0.54)</td>
<td>0.94 (0.77, 1.15)</td>
</tr>
</tbody>
</table>

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

LANTUS (insulin glargine injection) is supplied as a clear solution containing 100 units per mL (U-100) of insulin glargine and is available in:

- Carton of one 10 mL multiple-dose vial NDC 0088-2220-33
- Carton of five 3 mL single-patient-use SoloStar pens NDC 0088-2219-05

The LANTUS SoloStar prefilled pen dials in 1-unit increments. Needles are not included in the packs.

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

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

16.2 Storage

LANTUS should not be stored in the freezer and should not be allowed to freeze. Discard LANTUS if it has been frozen. Protect LANTUS from direct heat and light. Storage conditions are summarized in the following table.

<table>
<thead>
<tr>
<th>Storage Condition</th>
<th>Not in-use (unopened)</th>
<th>Not in-use (unopened)</th>
<th>In-use (opened)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refrigerated (36°F–46°F [2°C–8°C])</td>
<td>Until expiration date</td>
<td>28 days</td>
<td>(See Temperature Below)</td>
</tr>
<tr>
<td>Room Temperature below 86°F (30°C)</td>
<td></td>
<td>28 days</td>
<td>Refrigerated or room temperature</td>
</tr>
<tr>
<td>10 mL Vial</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 mL SoloStar prefilled pen</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

 Patients

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LANTUS, TOUJEO and SoloStar are registered trademarks of sanofi-aventis U.S. LLC.

Do not share your syringes with other people, even if the needle has been changed. You may give other people a serious infection, or get a serious infection from them.

What is LANTUS?

LANTUS is a long-acting man-made-insulin used to control high blood sugar in adults with diabetes mellitus.

- LANTUS is not for use to treat diabetic ketoacidosis.
- It is not known if LANTUS is safe and effective in children less than 6 years of age with type 1 diabetes.
- It is not known if LANTUS is safe and effective in children with type 2 diabetes.

Who should not use LANTUS?

Do not use LANTUS if you:

- are having an episode of low blood sugar (hypoglycemia)
- have an allergy to insulin glargine or any of the ingredients in LANTUS.

See the end of this Patient Information leaflet for a complete list of ingredients in LANTUS.
What should I tell my healthcare provider before using LANTUS?
Before using LANTUS, tell your healthcare provider about all your medical conditions including if you:
- have liver or kidney problems
- take other medicines, especially ones called TZDs (thiazolidinediones)
- have heart failure or other heart problems. If you have heart failure, it may get worse while you take TZDs with LANTUS.
- are pregnant, planning to become pregnant, or are breastfeeding. It is not known if LANTUS may harm your unborn baby or breastfeeding baby.
Tell your healthcare provider about all the medicines you take including prescription and over-the-counter medicines, vitamins, and herbal supplements.
Before you start using LANTUS, talk to your healthcare provider about low blood sugar and how to manage it.

How should I use LANTUS?
- Read the detailed Instructions for Use that come with your LANTUS insulin.
- Use LANTUS exactly as your healthcare provider tells you to. Your healthcare provider should tell you how much LANTUS to use and when to use it.
- Know the amount of LANTUS you use. Do not change the amount of LANTUS you use unless your healthcare provider tells you to.
- Check your insulin label each time you give your injection to make sure you are using the correct insulin.
- Do not re-use needles. Always use a new needle for each injection. Re-use of needles increases your risk of having blocked needles, which may cause you to get the wrong dose of LANTUS. Using a new needle for each injection lowers your risk of getting an infection.
- 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.
- LANTUS is injected under your skin (subcutaneously). Do not use LANTUS in an insulin pump or inject LANTUS into your vein (intravenously).
- Change (rotate) injection sites within the area you chose with each dose. Do not use the exact spot for each injection.
- Do not mix LANTUS with any other type of insulin or liquid medicine.
- Check your blood sugar levels. Ask your healthcare provider what your blood sugar should be and when you should check your blood sugar levels.
Keep LANTUS and all medicines out of the reach of children.

What are the possible side effects of LANTUS and other insulins?
LANTUS may cause serious side effects that can lead to death, including:
- low blood sugar (hypoglycemia). Signs and symptoms that may indicate low blood sugar include:
  - dizziness or light-headedness, sweating, confusion, headache, blurred vision, slurred speech, shakiness, fast heartbeat, anxiety, irritability or mood change, hunger
- severe allergic reaction (whole body reaction). Get medical help right away if you have any of these signs or symptoms of a severe allergic reaction:
  - a rash over your whole body, trouble breathing, a fast heartbeat, or sweating
- low potassium in your blood (hypokalemia).
- Heart failure. Taking certain diabetes pills called TZDs (thiazolidinediones) with LANTUS may cause heart failure in some people. This can happen even if you have never had heart failure or heart problems before. If you already have heart failure it may get worse while you take TZDs with LANTUS. Your healthcare provider should monitor you closely while you are taking TZDs with LANTUS. Tell your healthcare provider if you have any new or worse symptoms of heart failure including:
  - shortness of breath, swelling of your ankles or feet, sudden weight gain
Treatment with TZDs and LANTUS may need to be changed or stopped by your healthcare provider if you have new or worse heart failure.

Get emergency medical help if you have:
- trouble breathing; shortness of breath; fast heartbeat; swelling of your face, tongue, or throat; sweating; extreme drowsiness; dizziness; confusion.

The most common side effects of LANTUS include:
- low blood sugar (hypoglycemia); weight gain; allergic reactions, including reactions at your injection site; skin thickening or pits at the injection site (lipodystrophy).

These are not all the possible side effects of LANTUS. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of LANTUS.
Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use LANTUS for a condition for which it was not prescribed. It may harm them. This Patient Information leaflet summarizes the most important information about LANTUS. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about LANTUS that is written for healthcare professionals. For more information, go to www.lantus.com or call 1-800-633-1610.

What are the ingredients in LANTUS?
- Active ingredients: insulin glargine
- 10 ml vial inactive ingredients: zinc, m-cresol, glycerol, polysorbate, and water for injection

Manufactured By: sanofi-aventis U.S. LLC, Bridgewater, NJ 08807

This Patient Information has been approved by the U.S. Food and Drug Administration
Approved: July/2015
Instructions for Use
LANTUS® (LAN-tus)
(insulin glargine injection) for subcutaneous use
10 mL Vial (100 Units/mL, U-100)
Read the Instructions for Use before you start taking LANTUS and each time you get a new LANTUS vial. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.
Do not share your LANTUS syringes with other people even if the needle has been changed. You may give other people a serious infection, or get a serious infection from them.
Supplies needed to give your injection:
• a LANTUS 10 mL vial
• a U-100 insulin syringe and needle
• 2 alcohol swabs
• 1 sharps container for throwing away used needles and syringes.
See “Disposing of used needles and syringes” at the end of these instructions.
Preparing your LANTUS dose:
• Wash your hands with soap and water or with alcohol.
• Check the LANTUS label to make sure you are taking the right type of insulin. This is especially important if you use more than 1 type of insulin.
• Check the insulin to make sure it is clear and colorless. Do not use LANTUS if it is colored or cloudy, or if you see particles in the solution.
• Do not use LANTUS after the expiration date stamped on the label or 28 days after you first use it.
• Always use a syringe that is marked for U-100 insulin. If you use a syringe other than a U-100 insulin syringe, you may get the wrong dose of insulin.
• Always use a new syringe or needle for each injection. Do not reuse or share your syringes or needles with other people. You may give other people a serious infection or get a serious infection from them.
Step 1:
If you are using a new vial, remove the protective cap. Do not remove the stopper.
Step 2:
Wipe the top of the vial with an alcohol swab. You do not have to shake the vial of LANTUS before use.
Step 3:
Draw air into the syringe equal to your insulin dose. Put the needle through the rubber top of the vial and push the plunger to inject the air into the vial.
Step 4:
Leave the syringe in the vial and turn both upside down. Hold the syringe and vial firmly in one hand. Make sure the tip of the needle is in the insulin. With your free hand, pull the plunger to withdraw the correct dose into the syringe.
Step 5:
Before you take the needle out of the vial, check the syringe for air bubbles. If bubbles are in the syringe, hold the syringe straight up and tap the side of the syringe until the bubbles float to the top. Push the bubbles out with the plunger and draw insulin back in until you have the correct dose.
Step 6:
Remove the needle from the vial. Do not let the needle touch anything. You are now ready to inject.
Giving your LANTUS injection:
• Inject your insulin exactly as your healthcare provider has shown you.
• Change (rotate) your injection site for each injection.
Step 7:
Choosing your injection site: LANTUS is injected under the skin (subcutaneously) of your upper arm, thigh, or stomach area (abdomen). Wipe the skin with an alcohol swab to clean the injection site. Let the injection site dry before you inject your dose.
Step 8:
• Pinch the skin.
• Insert the needle in the way your healthcare provider showed you.
• Release the skin.
• Slowly push in the plunger of the syringe all the way, making sure you have injected all the insulin.
• Leave the needle in the skin for about 10 seconds.
Step 9:
• Pull the needle straight out of your skin.
• Gently press the injection site for several seconds. Do not rub the area.
• Do not recap the used needle. Recapping the needle can lead to a needle stick injury.
Disposing of used needles and syringes:
• Put your used needles and syringes in a FDA-cleared sharps disposal container right away after use. Do not throw away (dispose of ) loose needles and syringes in your household trash.
If you do not have a FDA-cleared sharps container, you may use a household container that is:
- made of a heavy-duty plastic,
- can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
- upright and stable during use,
- leak resistant, and
- properly labeled to warn of hazardous waste inside the container.

When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal.

Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. Do not recycle your used sharps disposal container.

How should I store LANTUS?
- Store unused LANTUS vials in the refrigerator between 36°F to 46°F (2°C to 8°C).
- Store in-use (opened) LANTUS vials in a refrigerator or at room temperature below 86°F (30°C).
- Do not freeze LANTUS.
- Keep LANTUS out of direct heat and light.
- If a vial has been frozen or overheated, throw it away.
- The LANTUS vials you are using should be thrown away after 28 days, even if it still has insulin left in it.

This Instructions for Use have been approved by the U.S. Food and Drug Administration. Revised: July/2015

<table>
<thead>
<tr>
<th>Patient Information</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LANTUS® (LAN-tus)</strong></td>
<td>(insulin glargine injection) for subcutaneous use, 100 Units/mL (U-100)</td>
</tr>
</tbody>
</table>

Do not share your LANTUS SoloStar® pen with other people, even if the needle has been changed. You may give other people a serious infection, or get a serious infection from them.

What is LANTUS?
LANTUS is a long-acting man-made insulin used to control high blood sugar in adults with diabetes mellitus.
- LANTUS is not for use to treat diabetic ketoacidosis.
- It is not known if LANTUS is safe and effective in children less than 6 years of age with type 1 diabetes.
- It is not known if LANTUS is safe and effective in children with type 2 diabetes.

Who should not use LANTUS?
Do not use LANTUS if you:
- are having an episode of low blood sugar (hypoglycemia)
- have an allergy to insulin glargine or any of the ingredients in LANTUS. See the end of this Patient Information leaflet for a complete list of ingredients in LANTUS.

What should I tell my healthcare provider before using LANTUS?
Before using LANTUS, tell your healthcare provider about all your medical conditions including if you:
- have liver or kidney problems
- take other medicines, especially ones called TZDs (thiazolidinediones)
- have heart failure or other heart problems. If you have heart failure, it may get worse while you take TZDs with LANTUS.
- are pregnant, planning to become pregnant, or are breastfeeding. It is not known if LANTUS may harm your unborn baby or breastfeeding baby.

Tell your healthcare provider about all the medicines you take including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Before you start using LANTUS, talk to your healthcare provider about low blood sugar and how to manage it.

How should I use LANTUS?
- Read the detailed Instructions for Use that come with your LANTUS SoloStar disposable prefilled pen.
- Use LANTUS exactly as your healthcare provider tells you to.
- Your healthcare provider should tell you how much LANTUS to use and when to use it.
- Know the amount of LANTUS you use. Do not change the amount of LANTUS you use unless your healthcare provider tells you to.
- Check your insulin label each time you give your injection to make sure you are using the correct insulin.
- LANTUS comes in a SoloStar disposable prefilled pen that you must use to give your LANTUS. The dose counter on your pen shows your dose of LANTUS. Do not make any dose changes unless your healthcare provider tells you to.
- Do not use a syringe to remove LANTUS from your SoloStar disposable prefilled pen.
- Do not re-use needles. Always use a new needle for each injection. Re-use of needles increases your risk of having blocked needles, which may cause you to get the wrong dose of LANTUS. Using a new needle for each injection lowers your risk of getting an infection. If your needle is blocked, follow the instructions in Step 3 of the Instructions for Use.
- You may take LANTUS at any time during the day but you must take it at the same time every day.
- LANTUS is injected under your skin (subcutaneously). Do not use LANTUS in an insulin pump or inject LANTUS into your vein (intravenously).
- Change (rotate) your injection sites within area you chose with each dose. Do not use the exact spot for each injection.
- Do not mix LANTUS with any other type of insulin or liquid medicine.
- Check your blood sugar levels. Ask your healthcare provider what your blood sugar should be and when you should check your blood sugar levels.

Keep LANTUS and all medicines out of the reach of children.

Your dose of LANTUS may need to change because of:
- a change in level of physical activity or exercise, weight gain or loss, increased stress, illness, change in diet, or because of the medicines you take.

What should I avoid while using LANTUS?
While using LANTUS do not:
- drive or operate heavy machinery, until you know how LANTUS affects you
- drink alcohol or use over-the-counter medicines that contain alcohol

Pen with other people,

While using LANTUS do not:
- have an allergy to insulin glargine or any of the ingredients in LANTUS. See the end of this Patient Information leaflet for a complete list of ingredients in LANTUS.
What are the possible side effects of LANTUS and other insulins?

LANTUS may cause serious side effects that can lead to death, including:

- **low blood sugar (hypoglycemia).** Signs and symptoms that may indicate low blood sugar include:
  - dizziness or light-headedness, sweating, confusion, headache, blurred vision, slurred speech, shakiness, fast heartbeat, anxiety, irritability or mood change, hunger

- **severe allergic reaction (whole body reaction).** Get medical help right away if you have any of these signs or symptoms of a severe allergic reaction:
  - a rash over your whole body, trouble breathing, a fast heartbeat, or sweating

- **low potassium in your blood (hypokalemia).**

- **Heart failure.** Taking certain diabetes pills called TZDs (thiazolidinediones) with LANTUS may cause heart failure in some people. This can happen even if you have never had heart failure or heart problems before. If you already have heart failure it may get worse while you take TZDs with LANTUS. Your healthcare provider should monitor you closely while you are taking TZDs with LANTUS. Tell your healthcare provider if you have any new or worse symptoms of heart failure including:
  - shortness of breath, swelling of your ankles or feet, sudden weight gain

  Treatment with TZDs and LANTUS may need to be changed or stopped by your healthcare provider if you have new or worse heart failure.

**Get emergency medical help if you have:**

- trouble breathing; shortness of breath; fast heartbeat; swelling of your face, tongue, or throat; sweating; extreme drowsiness; dizziness; confusion.

**The most common side effects of LANTUS include:**

- low blood sugar (hypoglycemia); weight gain; allergic reactions, including reactions at your injection site; skin thickening or pits at the injection site (lipodystrophy).

**These are not all the possible side effects of LANTUS.** Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

**General information about the safe and effective use of LANTUS.**

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. **Do not** use LANTUS for a condition for which it was not prescribed. **Do not** give LANTUS to other people, even if they have the same symptoms that you have. It may harm them.

This Patient Information 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 the website www.lantus.com.

**What are the ingredients in LANTUS?**

- **Active ingredient:** insulin glargine
- **3 mL SoloStar prefilled pen inactive ingredients:** zinc, m-cresol, glycerol, and water for injection

  Hydrochloric acid and sodium hydroxide may be added to adjust the pH.

Manufactured by: sanofi-aventis U.S. LLC Bridgewater, NJ 08807

This Patient Information has been approved by the U.S. Food and Drug Administration

Approved: 11/2018

GLA-FPLR-SL-NOV18 Rx Only