ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS
1. NAME OF THE MEDICINAL PRODUCT

Toujeo 300 units/ml solution for injection in a pre-filled pen

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains 300 units insulin glargine* (equivalent to 10.91 mg).

Each pen contains 1.5 ml of solution for injection, equivalent to 450 units.

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

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection (injection). SoloStar

Clear colourless solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of diabetes mellitus in adults.

4.2 Posology and method of administration

Posology

Toujeo is a basal insulin for once-daily administration at any time of the day, preferably at the same time every day.

The dose regimen (dose and timing) should be adjusted according to individual response.

In type 1 diabetes mellitus, Toujeo must be combined with short-/rapid-acting insulin to cover mealtime insulin requirements.

In patients with type 2 diabetes mellitus, Toujeo can also be given together with other anti-hyperglycaemic medicinal products.

The potency of this medicinal product is stated in units. These units are exclusive to Toujeo and are not the same as IU or the units used to express the potency of other insulin analogues (see section 5.1).

Flexibility in dosing time

When needed, patients can administer Toujeo up to 3 hours before or after their usual time of administration (see section 5.1).

Patients who forget a dose, should be advised to check their blood sugar and then resume their usual once-daily dosing schedule. Patients should be informed not to inject a double dose to make up for a forgotten dose.
**Initiation**

*Patients with type 1 diabetes mellitus*
Toujeo is to be used once-daily with meal-time insulin and requires individual dose adjustments.

*Patients with type 2 diabetes mellitus*
The recommended daily starting dose is 0.2 units/kg followed by individual dose adjustments.

**Switch between insulin glargine 100 units/ml and Toujeo**

Insulin glargine 100 units/ml and Toujeo are not bioequivalent and are not directly interchangeable.

- When switching from insulin glargine 100 units/ml to Toujeo, this can be done on a unit-to-unit basis, but a higher Toujeo dose (approximately 10-18%) may be needed to achieve target ranges for plasma glucose levels.
- When switching from Toujeo to insulin glargine 100 units/ml, the dose should be reduced (approximately by 20%) to reduce the risk of hypoglycaemia.

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

**Switch from other basal insulins to Toujeo**

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

- Switching from once-daily basal insulins to once-daily Toujeo can be done unit-to-unit based on the previous basal insulin dose.
- Switching from twice-daily basal insulins to once-daily Toujeo, the recommended initial Toujeo dose is 80% of the total daily dose of basal insulin that is being discontinued.

Patients with high insulin doses because of antibodies to human insulin may experience an improved insulin response with Toujeo.

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

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

**Switch from Toujeo to other basal insulins**

Medical supervision with close metabolic monitoring is recommended during the switch and in the initial weeks thereafter.

Please refer to the prescribing information of the medicinal product to which the patient is switching.

**Special populations**

Toujeo can be used in elderly people, renal and hepatic impaired patients.

*Elderly population (≥65 years old)*
In the elderly, progressive deterioration of renal function may lead to a steady decrease in insulin requirements (see section 4.8 and 5.1).
**Renal impairment**

In patients with renal impairment, insulin requirements may be diminished due to reduced insulin metabolism (see section 4.8).

**Hepatic impairment**

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

**Paediatric population**

The safety and efficacy of Toujeo in children and adolescents below 18 years of age have not been established. No data are available.

**Method of administration**

Toujeo is for subcutaneous use only.

Toujeo is administered subcutaneously by injection in the abdominal wall, the deltoid or the thigh. Injection sites must be rotated within a given injection area from one injection to the next (see section 4.8).

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

Toujeo must not be used in insulin infusion pumps.

Before using Toujeo SoloStar pre-filled pen, the instructions for use included in the package leaflet must be read carefully (see section 6.6).

With Toujeo SoloStar pre-filled pen, a dose of 1-80 units per injection, in steps of 1 unit, can be injected. The dose window shows the number of Toujeo units to be injected. The Toujeo SoloStar pre-filled pen has been specifically designed for Toujeo, therefore no dose re-calculation is required.

Toujeo must not be drawn from the cartridge of the SoloStar pre-filled pen into a syringe or severe overdose can result (see section 4.4, 4.9 and 6.6).

A new sterile needle must be attached before each injection. Re-use of needles increases the risk of blocked needles which may cause underdosing or overdosing (see section 4.4 and 6.6).

To prevent possible transmission of disease, insulin pens should never be used for more than one person, even when the needle is changed (see section 6.6).

**4.3 Contraindications**

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

**4.4 Special warnings and precautions for use**

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

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

**Hypoglycaemia**

The time of occurrence of hypoglycaemia depends on the action profile of the insulins used and may, therefore, change when the treatment regimen is changed.
Particular caution should be exercised, and intensified blood glucose monitoring is advisable in patients in whom hypoglycaemic episodes might be of particular clinical relevance, such as in patients with significant stenoses of the coronary arteries or of the blood vessels supplying the brain (risk of cardiac or cerebral complications of hypoglycaemia) as well as in patients with proliferative retinopathy, particularly if not treated with photocoagulation (risk of transient amaurosis following hypoglycaemia).

Patients should be aware of circumstances where warning symptoms of hypoglycaemia are diminished. The warning symptoms of hypoglycaemia may be changed, be less pronounced or be absent in certain risk groups. These include patients:
- in whom glycaemic control is markedly improved,
- in whom hypoglycaemia develops gradually,
- who are elderly,
- after transfer from animal insulin to human insulin,
- in whom an autonomic neuropathy is present,
- with a long history of diabetes,
- suffering from a psychiatric illness,
- receiving concurrent treatment with certain other medicinal products (see section 4.5).

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

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

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

Adherence of the patient to the dose and dietary regimen, correct insulin administration and awareness of hypoglycaemia symptoms are essential to reduce the risk of hypoglycaemia. Factors increasing the susceptibility to hypoglycaemia require particularly close monitoring and may necessitate dose adjustment. These factors include:
- change in the injection area,
- improved insulin sensitivity (e.g., by removal of stress factors),
- unaccustomed, increased or prolonged physical activity,
- intercurrent illness (e.g. vomiting, diarrhoea),
- inadequate food intake,
- missed meals,
- alcohol consumption,
- certain uncompensated endocrine disorders, (e.g. in hypothyroidism and in anterior pituitary or adrenocortical insufficiency),
- concomitant treatment with certain other medicinal products (see section 4.5).

Switch between insulin glargine 100 units/ml and Toujeo
Since insulin glargine 100 units/ml and Toujeo are not bioequivalent and are not interchangeable, switching may result in the need for a change in dose and should only be done under strict medical supervision (see section 4.2).

Switch between other insulins and Toujeo
Switching a patient between another type or brand of insulin and Toujeo should be done under strict medical supervision. Changes in strength, brand (manufacturer), type (regular, NPH, lente, long-acting, etc.), origin (animal, human, human insulin analogue) and/or method of manufacture may result in the need for a change in dose (see section 4.2).

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

**Insulin antibodies**

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

**Combination of Toujeo with pioglitazone**

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

**Medication errors prevention**

Medication errors have been reported in which other insulins, particularly rapid-acting insulins, have been accidentally administered instead of long-acting insulins. Insulin label must always be checked before each injection to avoid medication errors between Toujeo and other insulins (see section 6.6).

To avoid dosing errors and potential overdose, the patients must be instructed to never use a syringe to remove Toujeo (insulin glargine 300 units/ml) from the SoloStar pre-filled pen (see section 4.9 and 6.6)

A new sterile needle must be attached before each injection. Patients must also be instructed to not re-use needles. Re-use of needles increases the risk of blocked needles which may cause underdosing or overdosing. In the event of blocked needle, the patients must follow the instructions described in Step 3 of the Instructions for Use accompanying the package leaflet (see section 6.6).

Patients must visually verify the number of selected units on the dose counter of the pen. Patients who are blind or have poor vision should be instructed to get help/assistance from another person who has good vision and is trained in using the insulin device.

See also section 4.2 under “Method of administration”.

**Excipients**

This medicinal product contains less than 1 mmol (23 mg) sodium per dose, i.e. it is essentially ‘sodium-free’.

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

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

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

Substances that may reduce the blood-glucose-lowering effect include corticosteroids, danazol, diazoxide, diuretics, glucagon, isoniazid, oestrogens and progestogens, phenothiazine derivatives, somatropin, sympathomimetic medicinal products (e.g. epinephrine [adrenaline], salbutamol, terbutaline), thyroid hormones, atypical antipsychotic medicinal products (e.g. clozapine and olanzapine) and protease inhibitors.
Beta-blockers, clonidine, lithium salts or alcohol may either potentiate or weaken the blood-glucose-lowering effect of insulin. Pentamidine may cause hypoglycaemia, which may sometimes be followed by hyperglycaemia.

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

4.6 Fertility, pregnancy and lactation

Pregnancy
There is no clinical experience with use of Toujeo in pregnant women.

For insulin glargine no clinical data on exposed pregnancies from controlled clinical studies are available. A large amount of data on pregnant women (more than 1,000 pregnancy outcomes with a medicinal product containing insulin glargine 100 units/ml) indicate no specific adverse effects on pregnancy and no specific malformative nor foeto/neonatal toxicity of insulin glargine. Animal data do not indicate reproductive toxicity. The use of Toujeo may be considered during pregnancy, if clinically needed.

It is essential for patients with pre-existing or gestational diabetes to maintain good metabolic control throughout pregnancy to prevent adverse outcomes associated with hyperglycemia. Insulin requirements may decrease during the first trimester and generally increase during the second and third trimesters. Immediately after delivery, insulin requirements decline rapidly (increased risk of hypoglycaemia). Careful monitoring of glucose control is essential.

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

Fertility
Animal studies do not indicate direct harmful effects with respect to fertility.

4.7 Effects on ability to drive and use machines

The patient's ability to concentrate and react may be impaired as a result of hypoglycaemia or hyperglycaemia or, for example, as a result of visual impairment. This may constitute a risk in situations where these abilities are of special importance (e.g. driving a car or using machines).

Patients should be advised to take precautions to avoid hypoglycaemia whilst driving. This is particularly important in those who have reduced or absent awareness of the warning symptoms of hypoglycaemia or have frequent episodes of hypoglycaemia. It should be considered whether it is advisable to drive or use machines in these circumstances.

4.8 Undesirable effects

Summary of the safety profile
The following adverse reactions were observed during clinical studies conducted with Toujeo (see section 5.1) and during clinical experience with insulin glargine 100 units/ml. Hypoglycaemia, in general the most frequent adverse reaction of insulin therapy, may occur if the insulin dose is too high in relation to the insulin requirement.
Tabulated list of adverse reactions
The following related adverse reactions from clinical investigations are listed below by system organ class and in order of decreasing incidence (very common: ≥1/10; common: ≥1/100 to <1/10; uncommon: ≥1/1,000 to <1/100; rare: ≥1/10,000 to <1/1,000; very rare: ≥1/10,000 to <1/1,000; not known: cannot be estimated from the available data).

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

<table>
<thead>
<tr>
<th>MedDRA system organ classes</th>
<th>Very common</th>
<th>Common</th>
<th>Uncommon</th>
<th>Rare</th>
<th>Very rare</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune system disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metabolism and nutrition disorders</td>
<td>Hypoglycaemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Nervous system disorders</td>
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<tr>
<td>Eyes disorders</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>Lipohypertrophy</td>
<td>Lipatrophy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td></td>
<td></td>
<td></td>
<td>Myalgia</td>
<td></td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td>Injection site reactions</td>
<td></td>
<td></td>
<td>Oedema</td>
<td></td>
</tr>
</tbody>
</table>

Description of selected adverse reactions

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

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

Immune system disorders
Immediate-type allergic reactions to insulin are rare. Such reactions to insulin (including insulin glargine) or the excipients may, for example, be associated with generalised skin reactions, angio-oedema, bronchospasm, hypotension and shock, and may be life-threatening. In Toujeo clinical studies in adult patients, the incidence of allergic reactions was similar in Toujeo-treated patients (5.3%) and insulin glargine 100 units/ml-treated patients (4.5%).

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

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

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

**General disorders and administration site conditions**
Injection site reactions include redness, pain, itching, hives, swelling, or inflammation. Most minor reactions to insulins at the injection site usually resolve in a few days to a few weeks. In Toujeo clinical studies in adult patients, the incidence of injection site reactions was similar in Toujeo-treated patients (2.5%) and insulin glargine 100 units/ml-treated patients (2.8%).

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

**Paediatric population**
No clinical studies with Toujeo have been conducted in the paediatric population. Therefore, the safety profile of Toujeo has not been established.

**Other special populations**
Based on the results from clinical studies, the safety profile of Toujeo in elderly patients and in patients with renal impairment was similar to that of the overall population (see section 5.1).

**Reporting of suspected adverse reactions**
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

### 4.9 Overdose

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

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

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

### 5. PHARMACOLOGICAL PROPERTIES

#### 5.1 Pharmacodynamic properties

Pharmacoherapeutic group: Drugs used in diabetes, insulins and analogues for injection, long-acting. ATC Code: A10A E04.

**Mechanism of action**
The primary activity of insulin, including insulin glargine, is regulation of glucose metabolism. Insulin and its analogues lower blood glucose levels by stimulating peripheral glucose uptake, especially by skeletal muscle and fat, and by inhibiting hepatic glucose production. Insulin inhibits lipolysis in the adipocyte, inhibits proteolysis and enhances protein synthesis.
Pharmacodynamic effects
Insulin glargine is a human insulin analogue designed to have a low solubility at neutral pH. At pH 4, insulin glargine is completely soluble. After injection into the subcutaneous tissue, the acidic solution is neutralised leading to formation of a precipitate from which small amounts of insulin glargine are continuously released.

As observed in euglycemic clamp studies in patients with type 1 diabetes, the glucose lowering effect of Toujeo was more stable and prolonged in comparison with insulin glargine 100 units/ml after subcutaneous injection. Figure 1 shows results from a cross-over study in 18 patients with type 1 diabetes conducted for a maximum of 36 hours after injection. The effect of Toujeo was beyond 24 hours (up to 36 hours) at clinically relevant doses.

The more sustained release of insulin glargine from the Toujeo precipitate compared to insulin glargine 100 units/ml is attributable to the reduction of the injection volume by two thirds that results in a smaller precipitate surface area.

Figure 1: Activity profile at steady state in patients with type 1 diabetes in a 36-hour euglycaemic clamp study

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

Insulin receptor binding: In vitro studies indicate that the affinity of insulin glargine and its metabolites M1 and M2 for the human insulin receptor is similar to the one of human insulin.

IGF-1 receptor binding: The affinity of insulin glargine for the human IGF-1 receptor is approximately 5 to 8-fold greater than that of human insulin (but approximately 70 to 80-fold lower than the one of IGF-1), whereas M1 and M2 bind the IGF-1 receptor with slightly lower affinity compared to human insulin.

The total therapeutic insulin concentration (insulin glargine and its metabolites) found in type 1 diabetic patients was markedly lower than what would be required for a halfmaximal occupation of the IGF-1 receptor and the subsequent activation of the mitogenic-proliferative pathway initiated by the IGF-1 receptor. Physiological concentrations of endogenous IGF-1 may activate the mitogenic-proliferative pathway; however, the therapeutic concentrations found in insulin therapy, including in Toujeo therapy, are considerably lower than the pharmacological concentrations required to activate the IGF-1 pathway.

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

Clinical efficacy and safety
The overall efficacy and safety of Toujeo (insulin glargine 300 units/ml) once-daily on glycaemic control was compared to that of once-daily insulin glargine 100 units/ml in open-label, randomised, active-control, parallel studies of up to 26 weeks of duration, including 546 patients with type 1 diabetes mellitus and 2,474 patients with type 2 diabetes mellitus (Table 1 and 2).

Results from all clinical trials with Toujeo indicated that reductions in HbA1c from baseline to end of trial were non-inferior to insulin glargine 100 units/ml. Plasma glucose reductions at the end of the trial with Toujeo were similar to insulin glargine 100 units/ml with a more gradual reduction during the titration period with Toujeo. Glycaemic control was similar when Toujeo was administered once daily in the morning or in the evening.

Improvement in HbA1C was not affected by, gender, ethnicity, age, diabetes duration (<10 years and ≥10 years), HbA1c value at baseline (<8% or ≥8%) or baseline body mass index (BMI). At the end of these treat-to-target trials, depending on the patient population and concomitant therapy, a 10-18% higher dose was observed in the Toujeo group than in the comparator group (Table 1 and 2).

Results from clinical trials demonstrated that the incidence of confirmed hypoglycaemia (at any time of the day and nocturnal) was lower in patients treated with Toujeo compared to insulin glargine 100 units/ml-treated patients, in patients with type 2 diabetes treated in combination with either non-insulin anti-hyperglycaemic medicinal product or mealtime insulin.

The superiority of Toujeo over insulin glargine 100 units/ml in lowering the risk of confirmed nocturnal hypoglycaemia was shown in patients with type 2 diabetes treated with basal insulin in combination with either non-insulin anti-hyperglycaemic medicinal product (18% risk reduction) or mealtime insulin (21% risk reduction) during the period from week 9 to end of study period. Overall, these effects on hypoglycaemia risk were consistently observed whatever the age, gender, BMI and duration of diabetes (<10 years and ≥10 years) in Toujeo-treated patients compared to insulin glargine 100 units/ml-treated patients.

In patients with type 1 diabetes, the incidence of hypoglycaemia was similar in patients treated with Toujeo compared to insulin glargine 100 units/ml-treated patients (Table 3).
### Table 1: Results from clinical trials in type 1 diabetes mellitus

<table>
<thead>
<tr>
<th>26 weeks of treatment</th>
<th>Toujeo</th>
<th>IGLar</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment in combination with</td>
<td>Meal-time insulin analogue</td>
<td></td>
</tr>
<tr>
<td>Number of subjects treated (mITT&lt;sup&gt;a&lt;/sup&gt;)</td>
<td>273</td>
<td>273</td>
</tr>
</tbody>
</table>

**HbA1c**

<table>
<thead>
<tr>
<th></th>
<th>Toujeo</th>
<th>IGLar</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline mean</td>
<td>8.13</td>
<td>8.12</td>
</tr>
<tr>
<td>Adjusted Mean change from baseline</td>
<td>-0.40</td>
<td>-0.44</td>
</tr>
<tr>
<td>Adjusted Mean difference&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.04 [-0.098 to 0.185]</td>
<td></td>
</tr>
</tbody>
</table>

**Basal insulin dose<sup>c</sup> (U/kg)**

<table>
<thead>
<tr>
<th></th>
<th>Toujeo</th>
<th>IGLar</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline mean</td>
<td>0.32</td>
<td>0.32</td>
</tr>
<tr>
<td>Mean change from baseline</td>
<td>0.15</td>
<td>0.09</td>
</tr>
</tbody>
</table>

**Body weight<sup>d</sup> (kg)**

<table>
<thead>
<tr>
<th></th>
<th>Toujeo</th>
<th>IGLar</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline mean</td>
<td>81.89</td>
<td>81.80</td>
</tr>
<tr>
<td>Mean change from baseline</td>
<td>0.46</td>
<td>1.02</td>
</tr>
</tbody>
</table>

IGlar: Insulin glargine 100 units/ml

- <sup>a</sup> mITT: Modified intention-to-treat
- <sup>b</sup> Treatment difference: Toujeo– insulin glargine 100 units/ml; [95% Confidence Interval]
- <sup>c</sup> Change from baseline to Month 6 (observed case)
- <sup>d</sup> Change from baseline to Last main 6-month on-treatment value

### Table 2: Results from clinical trials in type 2 diabetes mellitus

<table>
<thead>
<tr>
<th>26 weeks of treatment</th>
<th>Patients previously treated with basal insulin</th>
<th>Patients previously treated with basal insulin</th>
<th>Previously insulin naive patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment in combination with</td>
<td>Meal-time insulin analog +/- metformin</td>
<td>Non-insulin anti-hyperglycaemic medicinal products</td>
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</tr>
<tr>
<td></td>
<td>Toujeo</td>
<td>IGLar</td>
<td>Toujeo</td>
</tr>
<tr>
<td>Number of patients treated&lt;sup&gt;a&lt;/sup&gt;</td>
<td>404</td>
<td>400</td>
<td>403</td>
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</tbody>
</table>

**HbA1c**

<table>
<thead>
<tr>
<th></th>
<th>Toujeo</th>
<th>IGLar</th>
<th>Toujeo</th>
<th>IGLar</th>
<th>Toujeo</th>
<th>IGLar</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline mean</td>
<td>8.13</td>
<td>8.14</td>
<td>8.27</td>
<td>8.22</td>
<td>8.49</td>
<td>8.58</td>
</tr>
<tr>
<td>Adjusted mean change from baseline</td>
<td>-0.90</td>
<td>-0.87</td>
<td>-0.73</td>
<td>-0.70</td>
<td>-1.42</td>
<td>-1.46</td>
</tr>
<tr>
<td>Adjusted mean difference&lt;sup&gt;b&lt;/sup&gt;</td>
<td>-0.03 [-0.144 to 0.083]</td>
<td>-0.03 [-0.168 to 0.099]</td>
<td>0.04 [-0.090 to 0.174]</td>
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</tr>
</tbody>
</table>

**Basal insulin dose<sup>c</sup> (U/kg)**

<table>
<thead>
<tr>
<th></th>
<th>Toujeo</th>
<th>IGLar</th>
<th>Toujeo</th>
<th>IGLar</th>
<th>Toujeo</th>
<th>IGLar</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline mean</td>
<td>0.67</td>
<td>0.67</td>
<td>0.64</td>
<td>0.66</td>
<td>0.19</td>
<td>0.19</td>
</tr>
<tr>
<td>Mean change from baseline</td>
<td>0.31</td>
<td>0.22</td>
<td>0.30</td>
<td>0.19</td>
<td>0.43</td>
<td>0.34</td>
</tr>
</tbody>
</table>

**Body weight<sup>d</sup> (kg)**

<table>
<thead>
<tr>
<th></th>
<th>Toujeo</th>
<th>IGLar</th>
<th>Toujeo</th>
<th>IGLar</th>
<th>Toujeo</th>
<th>IGLar</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline mean</td>
<td>106.11</td>
<td>106.50</td>
<td>98.73</td>
<td>98.17</td>
<td>95.14</td>
<td>95.65</td>
</tr>
<tr>
<td>Mean change from baseline</td>
<td>0.93</td>
<td>0.90</td>
<td>0.08</td>
<td>0.66</td>
<td>0.50</td>
<td>0.71</td>
</tr>
</tbody>
</table>
IGlar: Insulin glargine 100 units/ml

- mITT: Modified intention-to-treat
- Treatment difference: Toujeo– insulin glargine 100 units/ml; [95% Confidence Interval]
- Change from baseline to Month 6 (observed case)
- Change from baseline to Last main 6-month on-treatment value

Table 3 - Summary of the hypoglycaemic episodes of the clinical study in patients with type 1 and type 2 diabetes mellitus

<table>
<thead>
<tr>
<th>Diabetic population</th>
<th>Type 1 diabetes mellitus</th>
<th>Type 2 diabetes mellitus</th>
<th>Type 2 diabetes mellitus</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients previously</td>
<td>Patients previously</td>
<td>Patients previously</td>
</tr>
<tr>
<td></td>
<td>treated with basal</td>
<td>treated with basal</td>
<td>treated with basal</td>
</tr>
<tr>
<td></td>
<td>insulin</td>
<td>insulin</td>
<td>insulin</td>
</tr>
<tr>
<td>Treatment in</td>
<td>Meal-time insulin analog</td>
<td>Meal-time insulin analog</td>
<td>Non-insulin anti-</td>
</tr>
<tr>
<td>combination with</td>
<td></td>
<td></td>
<td>hyperglycaemic</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>medicinal products</td>
</tr>
<tr>
<td>Toujeo</td>
<td>IGlar</td>
<td>Toujeo</td>
<td>IGlar</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Incidence (%) of severe a hypoglycaemia (n/Total N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entire study period d</td>
</tr>
<tr>
<td>6.6 (18/274)</td>
</tr>
<tr>
<td>9.5 (26/275)</td>
</tr>
<tr>
<td>5.0 (20/404)</td>
</tr>
<tr>
<td>5.7 (23/402)</td>
</tr>
<tr>
<td>1.0 (8/838)</td>
</tr>
<tr>
<td>1.2 (10/844)</td>
</tr>
<tr>
<td>RR*: 0.69 [0.39;1.23]</td>
</tr>
<tr>
<td>RR: 0.87 [0.48;1.55]</td>
</tr>
<tr>
<td>RR: 0.82 [0.33;2.00]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Incidence (%) of confirmed b hypoglycaemia (n/Total N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entire study period</td>
</tr>
<tr>
<td>93.1 (255/274)</td>
</tr>
<tr>
<td>93.5 (257/275)</td>
</tr>
<tr>
<td>81.9 (331/404)</td>
</tr>
<tr>
<td>87.8 (353/402)</td>
</tr>
<tr>
<td>57.6 (483/838)</td>
</tr>
<tr>
<td>64.5 (544/844)</td>
</tr>
<tr>
<td>RR: 1.00 [0.95;1.04]</td>
</tr>
<tr>
<td>RR: 0.93 [0.88; 0.99]</td>
</tr>
<tr>
<td>RR: 0.89 [0.83; 0.96]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Incidence (%) of confirmed nocturnal c hypoglycaemia (n/Total N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>From week 9 to end of study period</td>
</tr>
<tr>
<td>59.3 (162/273)</td>
</tr>
<tr>
<td>56.0 (153/273)</td>
</tr>
<tr>
<td>36.1 (146/404)</td>
</tr>
<tr>
<td>46.0 (184/400)</td>
</tr>
<tr>
<td>18.4 (154/835)</td>
</tr>
<tr>
<td>22.5 (188/835)</td>
</tr>
<tr>
<td>RR: 1.06 [0.92;1.23]</td>
</tr>
<tr>
<td>RR: 0.79 [0.67;0.93]</td>
</tr>
<tr>
<td>RR: 0.82 [0.68;0.99]</td>
</tr>
</tbody>
</table>

IGlar: Insulin glargine 100 units/ml

- a Severe hypoglycaemia: Episode requiring assistance of another person to actively administer carbohydrate, glucagon, or other resuscitative actions.
- b Confirmed hypoglycaemia: Any severe hypoglycaemia and/or hypoglycaemia confirmed by plasma glucose value ≤3.9 mmol/l.
- c Nocturnal hypoglycaemia: Episode that occurred between 00:00 and 05:59 hours
- d 6-month treatment period
- *RR: estimated risk ratio; [95% Confidence Interval]

**Flexibility in dosing time**

The safety and efficacy of Toujeo administered with a fixed or flexible dosing time were also evaluated in 2 randomized, open-label clinical studies for 3 months. Type 2 diabetic patients (n=194) received Toujeo once daily in the evening, either at the same time of the day (fixed time of administration) or within 3 hours before or after the usual time of administration (flexible dosing time). Administration with a flexible dosing time had no effect on glycaemic control and the incidence of hypoglycaemia.
**Antibodies**

Results from studies comparing Toujeo and insulin glargine 100 units/ml did not indicate any difference in term of development of anti-insulin antibodies, on efficacy, safety or dose of basal insulin between Toujeo and insulin glargine 100 units/ml.

**Body weight**

Mean change in body weight of less than 1 kg at the end of the 6-month period was observed in Toujeo-treated patients (see Table 1 and 2).

**Results from a study on progression of diabetic retinopathy**

Effects of insulin glargine 100 units/ml (once daily) on diabetic retinopathy were evaluated in an open-label 5 year NPH-controlled study (NPH given bid) in 1024 type 2 diabetic patients in which progression of retinopathy by 3 or more steps on the Early Treatment Diabetic Retinopathy Study (ETDRS) scale was investigated by fundus photography. No significant difference was seen in the progression of diabetic retinopathy when insulin glargine100 units/ml was compared to NPH insulin.

**Long term efficacy and safety outcome study**

The ORIGIN (Outcome Reduction with Initial Glargine INtervention) study was a multicenter, randomized, 2x2 factorial design study conducted in 12,537 participants at high cardiovascular (CV) risk with impaired fasting glucose (IFG) or impaired glucose tolerance (IGT) (12% of participants) or type 2 diabetes mellitus (treated with ≤1 antidiabetic oral agent) (88% of participants). Participants were randomized (1:1) to receive insulin glargine 100 units/ml (n=6264), titrated to reach FPG ≤95 mg/dl (5.3 mM), or standard care (n=6273).

The first co-primary efficacy outcome was the time to the first occurrence of CV death, nonfatal myocardial infarction (MI), or nonfatal stroke, and the second co-primary efficacy outcome was the time to the first occurrence of any of the first co-primary events, or revascularisation procedure (coronary, carotid, or peripheral), or hospitalisation for heart failure.

Secondary endpoints included all-cause mortality and a composite microvascular outcome.

Insulin glargine 100 units/ml did not alter the relative risk for CV disease and CV mortality when compared to standard of care. There were no differences between insulin glargine and standard care for the two co-primary outcomes; for any component endpoint comprising these outcomes; for all-cause mortality; or for the composite microvascular outcome.

Mean dose of insulin glargine 100 units/ml by study end was 0.42 U/kg. At baseline, participants had a median HbA1c value of 6.4% and median on-treatment HbA1c values ranged from 5.9 to 6.4% in the insulin glargine 100 units/ml group, and 6.2% to 6.6% in the standard care group throughout the duration of follow-up.

The rates of severe hypoglycaemia (affected participants per 100 participant years of exposure) were 1.05 for insulin glargine 100 units/ml and 0.30 for standard care group and the rates of confirmed non-severe hypoglycaemia were 7.71 for insulin glargine 100 units/ml and 2.44 for standard care group. Over the course of this 6-year study, 42% of the insulin glargine 100 units/ml group did not experience any hypoglycaemia.

At the last on-treatment visit, there was a mean increase in body weight from baseline of 1.4 kg in the insulin glargine 100 units/ml group and a mean decrease of 0.8 kg in the standard care group.
5.2 Pharmacokinetic properties

Absorption and distribution
In healthy subjects and diabetic patients, insulin serum concentrations indicated a slower and more prolonged absorption resulting in a flatter time-concentration profile after subcutaneous injection of Toujeo in comparison to insulin glargine 100 units/ml.

Pharmacokinetic profiles were consistent with the pharmacodynamic activity of Toujeo.

Steady state level within the therapeutic range is reached after 3-4 days of daily Toujeo administration.

After subcutaneous injection of Toujeo, the intra-subject variability, defined as the coefficient of variation for the insulin exposure during 24 hours was low at steady state (17.4%).

Biotransformation
After subcutaneous injection of insulin glargine, insulin glargine is rapidly metabolized at the carboxyl terminus of the Beta chain with formation of two active metabolites M1 (21A-Gly-insulin) and M2 (21A-Gly-des-30B-Thr-insulin). In plasma, the principal circulating compound is the metabolite M1. The exposure to M1 increases with the administered dose of insulin glargine. The pharmacokinetic and pharmacodynamic findings indicate that the effect of the subcutaneous injection with insulin glargine is principally based on exposure to M1. Insulin glargine and the metabolite M2 were not detectable in the vast majority of subjects and, when they were detectable their concentration was independent of the administered dose and formulation of insulin glargine.

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

The half-life after subcutaneous administration of Toujeo is determined by the rate of absorption from the subcutaneous tissue. The half-life of Toujeo after subcutaneous injection is 18-19 hours independent of dose.

5.3 Preclinical safety data

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

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Zinc chloride
Metacresol
Glycerol
Hydrochloric acid (for pH adjustment)
Sodium hydroxide (for pH adjustment)
Water for injections.

6.2 Incompatibilities

Toujeo must not be mixed or diluted with any other insulin or other medicinal products. Mixing or diluting Toujeo changes its time/action profile and mixing causes precipitation.

6.3 Shelf life

30 months.
Shelf life after first use of the pen

The medicinal product may be stored for a maximum of 6 weeks below 30°C and away from direct heat or direct light. Pens in use must not be stored in the refrigerator. The pen cap must be put back on the pen after each injection in order to protect from light.

6.4 Special precautions for storage

Before first use
Store in a refrigerator (2°C-8°C).
Do not freeze or place next to the freezer compartment or a freezer pack.
Keep the pre-filled pen in the outer carton in order to protect from light.

After first use or if carried as a spare

For storage conditions after first opening of this medicinal product, see section 6.3.

6.5 Nature and contents of container

Pre-filled pen
Cartridge (type 1 colourless glass) with a black plunger (bromobutyl rubber) and a flanged cap (aluminium) with a stopper (laminate of isoprene and bromobutyl rubber). The cartridge is sealed in a disposable pen injector. Each cartridge contains 1.5 ml solution.

Packs of 1, 3, 5 and 10 pens are available. Not all pack sizes may be marketed.
Needles are not included in the pack.

6.6 Special precautions for disposal and other handling

Before first use, the pen must be stored at room temperature at least 1 hour before use.

Before using Toujeo SoloStar pre-filled pen, the Instructions for Use included in the package leaflet must be read carefully. Toujeo SoloStar pre-filled pen has to be used as recommended in these Instructions for Use (see section 4.2).

The cartridge should be inspected before use. It must only be used if the solution is clear, colourless, with no solid particles visible, and if it is of water-like consistency. Since Toujeo is a solution, it does not require resuspension before use.

Insulin label must always be checked before each injection to avoid medication errors between Toujeo and other insulins. The strength “300” is highlighted in honey gold on the label (see section 4.4).

A syringe must never be used to withdraw Toujeo from the cartridge of the SoloStar pre-filled pen or severe overdose can result (see section 4.2, 4.4 and 4.9).

A new sterile needle must be attached before each injection. Needles must be discarded immediately after use. Needles must not be re-used. Re-use of needles increases the risk of blocked needles which may cause underdosing or overdosing. Using a new sterile needle for each injection also minimizes the risk of contamination and infection. In the event of blocked needle, the patients must follow the instructions described in Step 3 of the Instructions for Use accompanying the package leaflet (see section 4.2 and 4.4).

Used needles should be thrown away in a puncture resistant container or disposed of in accordance with local requirements.

Empty pens must never be reused and must be properly discarded.
To prevent possible transmission of disease, insulin pen should never be used by for more than one person, even when the needle is changed (see section 4.2).

7. MARKETING AUTHORISATION HOLDER
Sanofi-Aventis Deutschland GmbH, D-65926 Frankfurt am Main, Germany

8. MARKETING AUTHORISATION NUMBER(S)
EU/1/00/133/033
EU/1/00/133/034
EU/1/00/133/035
EU/1/00/133/036

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
Date of first authorisation: 27 June 2000
Date of latest renewal: 17 February 2015

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu
1. NAME OF THE MEDICINAL PRODUCT

Toujeo 100 units/ml solution for injection in a vial
Toujeo 100 units/ml solution for injection in a cartridge
Toujeo 100 units/ml solution for injection in a cartridge for OptiClik
Toujeo OptiSet 100 units/ml solution for injection in a pre-filled pen
Toujeo SoloStar 100 units/ml solution for injection in a pre-filled pen

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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

Vial
Each vial contains 5 ml of solution for injection, equivalent to 500 units, or 10 ml of solution for injection, equivalent to 1000 units.

Cartridge, cartridge for OptiClik, OptiSet pre-filled pen, SoloStar pre-filled pen
Each cartridge contains 3 ml of solution for injection, equivalent to 300 units

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

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

Clear colourless solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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

4.2 Posology and method of administration

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

The dose regimen (dose and timing) should be individually adjusted. In patients with type 2 diabetes mellitus, Toujeo can also be given together with orally active antidiabetic medicinal products.

The potency of this medicinal product is stated in units. These units are exclusive to Toujeo and are not the same as IU or the units used to express the potency of other insulin analogues (see section 5.1).

Special population
Elderly population (≥65 years old)
In the elderly, progressive deterioration of renal function may lead to a steady decrease in insulin requirements.

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

**Paediatric population**
- Adolescents and children aged 2 years and older patients
Safety and efficacy of Toujeo have been established in adolescents and children aged 2 years and older (see section 5.1). The dose regimen (dose and timing) should be individually adjusted.
- Children below 2 years of age
The safety and efficacy of Toujeo have not been established. No data are available.

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

To reduce the risk of nocturnal and early morning hypoglycaemia, patients who are changing their basal insulin regimen from a twice daily NPH insulin to a once daily regimen with Toujeo should reduce their daily dose of basal insulin by 20-30% during the first weeks of treatment. During the first weeks the reduction should, at least partially, be compensated by an increase in mealtime insulin, after this period the regimen should be adjusted individually.

Patients with high insulin doses because of antibodies to human insulin may experience an improved insulin response with Toujeo.

Close metabolic monitoring is recommended during the transition and in the initial weeks thereafter. With improved metabolic control and resulting increase in insulin sensitivity a further adjustment in dose regimen may become necessary. Dose adjustment may also be required, for example, if the patient's weight or life-style changes, change of timing of insulin dose or other circumstances arise that increase susceptibility to hypo- or hyperglycaemia (see section 4.4).

**Method of administration**
Toujeo is administered subcutaneously.

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

There are no clinically relevant differences in serum insulin or glucose levels after abdominal, deltoid or thigh administration of Toujeo. Injection sites must be rotated within a given injection area from one injection to the next.

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

**Vial, cartridge, cartridge for OptiClik**
For further details on handling, see section 6.6.

**OptiSet pre-filled pen, SoloStar pre-filled pen**
Before using the pre-filled pen, the instructions for use included in the package leaflet must be read carefully (see section 6.6).
4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

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

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

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

Hypoglycaemia

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

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

Patients should be aware of circumstances where warning symptoms of hypoglycaemia are diminished. The warning symptoms of hypoglycaemia may be changed, be less pronounced or be absent in certain risk groups. These include patients:
- in whom glycaemic control is markedly improved,
- in whom hypoglycaemia develops gradually,
- who are elderly,
- after transfer from animal insulin to human insulin,
- in whom an autonomic neuropathy is present,
- with a long history of diabetes,
- suffering from a psychiatric illness,
- receiving concurrent treatment with certain other medicinal products (see section 4.5).

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

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

If normal or decreased values for glycated haemoglobin are noted, the possibility of recurrent, unrecognised (especially nocturnal) episodes of hypoglycaemia must be considered.
Adherence of the patient to the dose and dietary regimen, correct insulin administration and awareness of hypoglycaemia symptoms are essential to reduce the risk of hypoglycaemia. Factors increasing the susceptibility to hypoglycaemia require particularly close monitoring and may necessitate dose adjustment. These include:
- change in the injection area,
- improved insulin sensitivity (e.g., by removal of stress factors),
- unaccustomed, increased or prolonged physical activity,
- intercurrent illness (e.g. vomiting, diarrhoea),
- inadequate food intake,
- missed meals,
- alcohol consumption,
- certain uncompensated endocrine disorders, (e.g. in hypothyroidism and in anterior pituitary or adrenocortical insufficiency),
- concomitant treatment with certain other medicinal products (see section 4.5).

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

Insulin antibodies
Insulin administration may cause insulin antibodies to form. In rare cases, the presence of such insulin antibodies may necessitate adjustment of the insulin dose in order to correct a tendency to hyper- or hypoglycaemia (see section 5.1).

Pens to be used with Toujeo cartridges
The Toujeo cartridges should only be used with the following pens:
- JuniorSTAR which delivers Toujeo in 0.5 unit dose increments
- OptiPen, ClikSTAR, Tactipen, Autopen 24 and AllStar, which all deliver Toujeo in 1 unit dose increments.
These cartridges should not be used with any other reusable pen as the dosing accuracy has only been established with the listed pens.
Not all of these pens may be marketed in your country

Handling of the OptiSet pre-filled pen and SoloStar pre-filled pen
Before using the pre-filled pen, the instructions for use included in the package leaflet must be read carefully. The pre-filled pens have to be used as recommended in these instructions for use (see section 6.6).

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

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

Excipients
This medicinal product contains less than 1 mmol (23 mg) sodium per dose, i.e. it is essentially ‘sodium-free’.
4.5 Interaction with other medicinal products and other forms of interaction

A number of substances affect glucose metabolism and may require dose adjustment of insulin glargine. Substances that may enhance the blood-glucose-lowering effect and increase susceptibility to hypoglycaemia include oral antidiabetic medicinal products, angiotensin converting enzyme (ACE) inhibitors, disopyramide, fibrates, fluoxetine, monoamine oxidase (MAO) inhibitors, pentoxifylline, propoxyphene, salicylates and sulfonamide antibiotics.

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

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

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

4.6 Fertility, pregnancy and lactation

Pregnancy
For insulin glargine no clinical data on exposed pregnancies from controlled clinical studies are available. A large amount of data on pregnant women (more than 1000 pregnancy outcomes) indicate no specific adverse effects of insulin glargine on pregnancy and no specific malformative nor feto/neonatal toxicity of insulin glargine. Animal data do not indicate reproductive toxicity. The use of Toujeo may be considered during pregnancy, if clinically needed.

It is essential for patients with pre-existing or gestational diabetes to maintain good metabolic control throughout pregnancy to prevent adverse outcomes associated with hyperglycaemia. Insulin requirements may decrease during the first trimester and generally increase during the second and third trimesters. Immediately after delivery, insulin requirements decline rapidly (increased risk of hypoglycaemia). Careful monitoring of glucose control is essential.

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

Fertility
Animal studies do not indicate direct harmful effects with respect to fertility.

4.7 Effects on ability to drive and use machines

The patient's ability to concentrate and react may be impaired as a result of hypoglycaemia or hyperglycaemia or, for example, as a result of visual impairment. This may constitute a risk in situations where these abilities are of special importance (e.g. driving a car or using machines).

Patients should be advised to take precautions to avoid hypoglycaemia whilst driving. This is particularly important in those who have reduced or absent awareness of the warning symptoms of hypoglycaemia or have frequent episodes of hypoglycaemia. It should be considered whether it is advisable to drive or use machines in these circumstances.
4.8 Undesirable effects

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

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

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

<table>
<thead>
<tr>
<th>MedDRA system organ classes</th>
<th>Very common</th>
<th>Common</th>
<th>Uncommon</th>
<th>Rare</th>
<th>Very rare</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune system disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Allergic reactions</td>
</tr>
<tr>
<td>Metabolism and nutrition disorders</td>
<td>Hypoglycaemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td></td>
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<td>Dysgeusia</td>
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<td>Visual impairment Retinopathy</td>
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<td>Skin and subcutaneous tissue disorders</td>
<td>Lipohypertrophy</td>
<td>Lipatrophy</td>
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<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td>Myalgia</td>
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<tr>
<td>General disorders and administration site conditions</td>
<td>Injection site reactions</td>
<td></td>
<td>Oedema</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Description of selected adverse reactions

Metabolism and nutrition disorders
Severe hypoglycaemic attacks, especially if recurrent, may lead to neurological damage. Prolonged or severe hypoglycaemic episodes may be life-threatening.
In many patients, the signs and symptoms of neuroglycopenia are preceded by signs of adrenergic counter-regulation. Generally, the greater and more rapid the decline in blood glucose, the more marked is the phenomenon of counter-regulation and its symptoms (see section 4.4).

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

Eyes disorders
A marked change in glycaemic control may cause temporary visual impairment, due to temporary alteration in the turgidity and refractive index of the lens.
Long-term improved glycaemic control decreases the risk of progression of diabetic retinopathy. However, intensification of insulin therapy with abrupt improvement in glycaemic control may be associated with temporary worsening of diabetic retinopathy. In patients with proliferative retinopathy, particularly if not treated with photocoagulation, severe hypoglycaemic episodes may result in transient amaurosis.

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

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

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

**Paediatric population**
In general, the safety profile for children and adolescents (≤18 years of age) is similar to the safety profile for adults. The adverse reaction reports received from post marketing surveillance included relatively more frequent injection site reactions (injection site pain, injection site reaction) and skin reactions (rash, urticaria) in children and adolescents (≤18 years of age) than in adults. Clinical study safety data are not available for children under 2 years.

**Reporting of suspected adverse reactions**
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

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

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

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Drugs used in diabetes, insulins and analogues for injection, long-acting. ATC Code: A10AE04.

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

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

Insulin receptor binding: In vitro studies indicate that the affinity of insulin glargine and its metabolites M1 and M2 for the human insulin receptor is similar to the one of human insulin.

IGF-1 receptor binding: The affinity of insulin glargine for the human IGF-1 receptor is approximately 5 to 8-fold greater than that of human insulin (but approximately 70 to 80-fold lower than the one of IGF-1), whereas M1 and M2 bind the IGF-1 receptor with slightly lower affinity compared to human insulin.

The total therapeutic insulin concentration (insulin glargine and its metabolites) found in type 1 diabetic patients was markedly lower than what would be required for a halfmaximal occupation of the IGF-1 receptor and the subsequent activation of the mitogenic-proliferative pathway initiated by the IGF-1 receptor. Physiological concentrations of endogenous IGF-1 may activate the mitogenic-proliferative pathway; however, the therapeutic concentrations found in insulin therapy, including in Toujeo therapy, are considerably lower than the pharmacological concentrations required to activate the IGF-1 pathway.

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

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

In euglycaemic clamp studies in healthy subjects or in patients with type 1 diabetes, the onset of action of subcutaneous insulin glargine was slower than with human NPH insulin, its effect profile was smooth and peakless, and the duration of its effect was prolonged.
The following graph shows the results from a study in patients:

**Activity profile in patients with type 1 diabetes**

* determined as amount of glucose infused to maintain constant plasma glucose levels (hourly mean values)

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

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

In clinical studies, antibodies that cross-react with human insulin and insulin glargine were observed with the same frequency in both NPH-insulin and insulin glargine treatment groups.

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

The ORIGIN (Outcome Reduction with Initial Glargine INtervention) study was a multicenter, randomised, 2x2 factorial design study conducted in 12,537 participants at high cardiovascular (CV) risk with impaired fasting glucose (IFG) or impaired glucose tolerance (IGT) (12% of participants) or type 2 diabetes mellitus treated with ≤1 antidiabetic oral agent (88% of participants). Participants were randomised (1:1) to receive insulin glargine (n=6264), titrated to reach FPG ≤95 mg/dl (5.3 mM), or standard care (n=6273).

The first co-primary efficacy outcome was the time to the first occurrence of CV death, nonfatal myocardial infarction (MI), or nonfatal stroke, and the second co-primary efficacy outcome was the time to the first occurrence of any of the first co-primary events, or revascularisation procedure (coronary, carotid, or peripheral), or hospitalisation for heart failure.

Secondary endpoints included all-cause mortality and a composite microvascular outcome.

Insulin glargine did not alter the relative risk for CV disease and CV mortality when compared to
standard of care. There were no differences between insulin glargine and standard care for the two co-primary outcomes; for any component endpoint comprising these outcomes; for all-cause mortality; or for the composite microvascular outcome.

Mean dose of insulin glargine by study end was 0.42 U/kg. At baseline, participants had a median HbA1c value of 6.4% and median on-treatment HbA1c values ranged from 5.9 to 6.4% in the insulin glargine group, and 6.2% to 6.6% in the standard care group throughout the duration of follow-up. The rates of severe hypoglycaemia (affected participants per 100 participant years of exposure) were 1.05 for insulin glargine and 0.30 for standard care group and the rates of confirmed non-severe hypoglycaemia were 7.71 for insulin glargine and 2.44 for standard care group. Over the course of this 6-year study, 42% of the insulin glargine group did not experience any hypoglycaemia.

At the last on-treatment visit, there was a mean increase in body weight from baseline of 1.4 kg in the insulin glargine group and a mean decrease of 0.8 kg in the standard care group.

Paediatric population
In a randomised, controlled clinical study, paediatric patients (age range 6 to 15 years) with type 1 diabetes (n=349) were treated for 28 weeks with a basal-bolus insulin regimen where regular human insulin was used before each meal. Insulin glargine was administered once daily at bedtime and NPH human insulin was administered once or twice daily. Similar effects on glycohemoglobin and the incidence of symptomatic hypoglycaemia were observed in both treatment groups, however fasting plasma glucose decreased more from baseline in the insulin glargine group than in the NPH group. There was less severe hypoglycaemia in the insulin glargine group as well. One hundred forty three of the patients treated with insulin glargine in this study continued treatment with insulin glargine in an uncontrolled extension study with mean duration of follow-up of 2 years. No new safety signals were seen during this extended treatment with insulin glargine.

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

A 24-week parallel group study was conducted in 125 children with type 1 diabetes mellitus aged 2 to 6 years, comparing insulin glargine given once daily in the morning to NPH insulin given once or twice daily as basal insulin. Both groups received bolus insulin before meals. The primary aim of demonstrating non-inferiority of insulin glargine to NPH in all hypoglycaemia was not met and there was a trend to an increase of hypoglycemic events with insulin glargine [insulin glargine: NPH rate ratio (95% CI) = 1.18 (0.97-1.44)]. Glycohaemoglobin and glucose variabilities were comparable in both treatment groups. No new safety signals were observed in this study.

5.2 Pharmacokinetic properties

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

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

When given intravenously the elimination half-life of insulin glargine and human insulin were comparable.
After subcutaneous injection of Toujeo in diabetic patients, insulin glargine is rapidly metabolized at the carboxyl terminus of the Beta chain with formation of two active metabolites M1 (21A-Gly-insulin) and M2 (21A-Gly-des-30B-Thr-insulin). In plasma, the principal circulating compound is the metabolite M1. The exposure to M1 increases with the administered dose of Toujeo. The pharmacokinetic and pharmacodynamic findings indicate that the effect of the subcutaneous injection with Toujeo is principally based on exposure to M1. Insulin glargine and the metabolite M2 were not detectable in the vast majority of subjects and, when they were detectable their concentration was independent of the administered dose of Toujeo.

In clinical studies, subgroup analyses based on age and gender did not indicate any difference in safety and efficacy in insulin glargine-treated patients compared to the entire study population.

**Paediatric population**
Pharmacokinetics in children aged 2 to less than 6 years with type 1 diabetes mellitus was assessed in one clinical study (see section 5.1). Plasma “trough” levels of insulin glargine and its main M1 and M2 metabolites were measured in children treated with insulin glargine, revealing plasma concentration patterns similar to adults, and providing no evidence for accumulation of insulin glargine or its metabolites with chronic dosing.

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

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

5ml vial, cartridge, cartridge for OtiClik, Optiset pre-filled pen, SoloStar pre-filled pen,
Zinc chloride
Metacresol
Glycerol
Hydrochloric acid (for pH adjustment)
Sodium hydroxide (for pH adjustment)
Water for injections

10ml vial
Zinc chloride
Metacresol
Glycerol
Hydrochloric acid (for pH adjustment)
Polysorbate 20
Sodium hydroxide (for pH adjustment)
Water for injections

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

Vial, cartridge, cartridge for OptiClik
It is important to ensure that syringes do not contain traces of any other material.
6.3 Shelf-life

Vial
5 ml vial
2 years.

10 ml vial
3 years.

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

10 ml vial
The medicinal product may be stored for a maximum of 4 weeks not above 30°C and away from direct heat or direct light. Keep the vial in the outer carton in order to protect from light.

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

Cartridge, cartridge for OptiClik, OptiSet pre-filled pen, SoloStar pre-filled pen:
3 years.

After first use
The medicinal product may be stored for a maximum of 4 weeks not above 30°C and away from direct heat or direct light. The pen containing a cartridge or the pens in use must not be stored in the refrigerator. The pen cap must be put back on the pen after each injection in order to protect from light.

6.4 Special precautions for storage

Before first use
Store in a refrigerator (2°C-8°C).
Do not freeze or place next to the freezer compartment or a freezer pack.
Keep the vial, cartridge or pre-filled pen in the outer carton in order to protect from light.

After first use
For storage conditions after first opening of this medicinal product, see section 6.3.

6.5 Nature and contents of container

Vial
Type 1 colourless glass vial with a flanged cap (aluminium), a stopper (chlorobutyl rubber (type 1)) and a tear-off cap (polypropylene) containing 5 ml of solution.
Packs of 1, 2, 5 and 10 vials.

Type 1 colourless glass vial with a flanged cap (aluminium), a stopper (type 1, laminate of polyisoprene and bromobutyl rubber) and a tear-off cap (polypropylene) containing 10 ml of solution. Pack of 1 vial.

Not all pack sizes may be marketed.
Cartridge, cartridge for OptiClik, OptiSet pre-filled pen, SoloStar pre-filled pen
Type 1 colourless glass cartridge with a black plunger (bromobutyl rubber) and a flanged cap (aluminium) with a stopper (bromobutyl or laminate of polyisoprene and bromobutyl rubber) containing 3 ml of solution.

**Cartridge for OptiClik:**
The glass cartridge is irreversibly integrated in a transparent container and assembled to a plastic mechanism with a threaded rod at one extremity.

**OptiSet prefilled pen, SoloStar pre-filled pen:**
The cartridge is sealed in a disposable pen injector. Needles are not included in the pack.

**Pack size**
Packs of 4, 5 and 10 cartridges.
Packs of 1, 3, 4, 5, 6, 8, 9 and 10 cartridges for OptiClik.
Packs of 1, 3, 4, 5, 6, 8, 9 and 10 OptiSet prefilled pens.
Packs of 1, 3, 4, 5, 6, 8, 9 and 10 SoloStar pre-filled pens.
Not all pack sizes may be marketed

### 6.6 Special precautions for disposal and other handling

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

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

Insulin label must always be checked before each injection to avoid medication errors between insulin glargine and other insulins (see section 4.4).

**Toujeo in a cartridge**

**Insulin pen**
The Toujeo cartridges are to be used only in conjunction with the pens: OptiPen, ClikSTAR, Autopen 24, Tactipen, AllStar or JuniorSTAR (see section 4.4). Not all of these pens may be marketed in your country.
The pen should be used as recommended in the information provided by the device manufacturer. The manufacturer’s instructions for using the pen must be followed carefully for loading the cartridge, attaching the needle, and administering the insulin injection.

If the insulin pen is damaged or not working properly (due to mechanical defects) it has to be discarded, and a new insulin pen has to be used.
If the pen malfunctions (see instructions for using the pen), the solution may be drawn from the cartridge into a syringe (suitable for an insulin with 100 units/ml) and injected.

**Cartridge**

Before insertion into the pen, the cartridge must be stored at room temperature for 1 to 2 hours. Air bubbles must be removed from the cartridge before injection (see instructions for using the pen). Empty cartridges must not be refilled.

**Toujeo in a cartridge for OptiClik**
The cartridges for OptiClik are to be used in conjunction with OptiClik only and as recommended in the information provided by the device manufacturer. The manufacturer’s instructions for using the pen must be followed carefully for loading the cartridge, attaching the needle, and administering the insulin injection.
If OptiClik is damaged or not working properly (due to mechanical defects) it has to be discarded, and a new OptiClik has to be used.
Before insertion into the pen, the cartridge must be stored at room temperature for 1 to 2 hours.
Air bubbles must be removed from the cartridge before injection (see instructions for using the pen). Empty cartridges must not be refilled. If the pen malfunctions (see instructions for using the pen), the solution may be drawn from the cartridge into a syringe (suitable for an insulin with 100 units/ml) and injected.

Toujeo in OptiSet pre-filled pen or SoloStar pre-filled pen
Before first use, the pre-pen must be stored at room temperature for 1 to 2 hours. Empty pre-filled pens must never be reused and must be properly discarded. To prevent the possible transmission of disease, each pen must be used by one patient only. Before using the pre-filled pen, the instructions for use included in the package leaflet must be read carefully.

7. MARKETING AUTHORISATION HOLDER
Sanofi-Aventis Deutschland GmbH, D-65926 Frankfurt am Main, Germany.

8. MARKETING AUTHORISATION NUMBER(S)
EU/1/00/133/001-004
EU/1/00/133/005-007
EU/1/00/133/008
EU/1/00/133/009-016
EU/1/00/133/017-024
EU/1/00/133/025-032

9. DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION
Date of first authorisation: 27 June 2000
Date of latest renewal: 17 February 2015

10. DATE OF REVISION OF THE TEXT
Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu
ANNEX II

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT
A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer of the biological active substance

Sanofi-Aventis Deutschland GmbH
Industriepark Höchst
Brüningstraße 50
D-65926 Frankfurt / Main
Germany

Name and address of the manufacturers responsible for batch release

Sanofi-Aventis Deutschland GmbH
Industriepark Höchst
Brüningstraße 50
D-65926 Frankfurt / Main
Germany

Alternative site 10 ml vials:

Sanofi S.p.A.
Località Valcanello
03012 Anagni (FR)
Italy

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

• Periodic Safety Update Reports

The requirements for submission of periodic safety update reports for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

• Risk Management Plan (RMP)

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.
An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

**Additional risk minimisation measures**

Prior to launch of Toujeo 300 units/ml in each Member State the Marketing Authorisation Holder (MAH) must agree the content and format of the educational programme, including communication media, distribution modalities, and any other aspects, with the National Competent Authority.

The MAH shall ensure that in each Member State where Toujeo 300 units/ml is marketed, all healthcare professionals (HCPs) who are expected to prescribe or dispense Toujeo 300 units/ml, as well as all patients or their carers who are expected to use Toujeo 300 units/ml, are provided with educational material to address the risk(s) of Medication error (switching between 100 units/ml and 300 units/ml without dose adjustment).

The educational materials for healthcare professionals shall contain the following key elements:

- That insulin glargine 100 units/ml and insulin glargine 300 units/ml (Toujeo 300 units/ml) are not bioequivalent and are therefore not interchangeable without dose adjustment.
- That dose adjustment is needed when patients are switched from one to the other strength:
- After titration, on average a 10-18% higher basal insulin dose are needed to achieve target ranges for plasma glucose levels when using the 300 units/ml formulation compared to the 100 units/ml formulation.
- Switching from the 300 units/ml to the 100 units/ml concentration results in an increased risk of hypoglycaemic events, mainly in the first week after the switch. To reduce the risk of hypoglycaemia, patients who are changing their basal insulin regimen from an insulin regimen with once daily Toujeo 300 units/ml (insulin glargine 300 units/ml) to a once daily regimen with insulin glargine 100 units/ml should reduce their dose by 20%;
- When switching from a treatment regimen with an intermediate or long-acting insulin product to a regimen with Toujeo 300 units/ml, a change of the dose of the basal insulin may be required and the concomitant anti-hyperglycaemic treatment may need to be adjusted. Close metabolic monitoring is recommended during the switch and in the initial weeks thereafter;
- Patients need to be instructed that insulin glargine 100 units/ml products and Toujeo are not interchangeable and dose adjustments need to be made;
- Blood glucose monitoring by patients is needed during the switch and the initial weeks thereafter;
- Reporting of medication errors or any side effects.

The educational material for patients and/or carers to address the risk(s) of Medication error (switching between 100 units/ml and 300 units/ml without dose adjustment) shall contain the following key elements:

- That insulin glargine 100 units/ml and insulin glargine 300 units/ml (Toujeo 300 units/ml) are not bioequivalent and are therefore not interchangeable without dose adjustment.
- That the switch from one insulin therapy to another should only be done when prescribed by their healthcare provider;
- That the dose newly recommended by their healthcare provider should always be followed;
- That blood glucose need to be closely monitored during the switch and the initial weeks thereafter;
- That they should consult their healthcare provider for further information;
- Reporting of medication errors or any side effects.

The target audience and the modalities for distribution of all of these materials are to be agreed at Member State Level. The MAH shall agree the final text and the context of the educational material.
for HCPs and patients together with a communication plan, with the National Competent Authority in each Member State prior to launch of the medicinal product.
ANNEX III

LABELLING AND PACKAGE LEAFLET
A. LABELLING
# PARTICULARS TO APPEAR ON THE OUTER PACKAGING

## OUTER CARTON

### 1. NAME OF THE MEDICINAL PRODUCT

Toujeo 300 units/ml solution for injection in a pre-filled pen insulin glargine

### 2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each ml contains 300 units (10.91 mg) insulin glargine. Each pen contains 1.5 ml of solution, equivalent to 450 units.

### 3. LIST OF EXCIPIENTS

Zinc chloride, metacresol, glycerol, hydrochloric acid / sodium hydroxide (for pH adjustment), water for injections

### 4. PHARMACEUTICAL FORM AND CONTENTS

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<thead>
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<th>Count</th>
<th>Description</th>
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</thead>
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<tr>
<td>1 pen</td>
<td>SoloStar solution for injection in a pre-filled pen</td>
</tr>
<tr>
<td>3 pens</td>
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</tr>
<tr>
<td>5 pens</td>
<td></td>
</tr>
<tr>
<td>10 pens</td>
<td></td>
</tr>
</tbody>
</table>

### 5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use. Open here Subcutaneous use

### 6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

### 7. OTHER SPECIAL WARNING(S), IF NECESSARY

Use only in this pen or severe overdose can result. Always use a new needle for each injection. For single patient use only. Use only clear and colourless solutions.

### 8. EXPIRY DATE
9. **SPECIAL STORAGE CONDITIONS**

Before first use
Store in a refrigerator.
Do not freeze or place next to the freezer compartment or a freezer pack.
Keep the pre-filled pen in the outer carton in order to protect from light.

After first use
The product may be stored for a maximum of 6 weeks below 30°C. Do not refrigerate. Put the pen cap back on the pen after each injection in order to protect from light.

10. **SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

11. **NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Sanofi-Aventis Deutschland GmbH
D-65926 Frankfurt am Main,
Germany.

12. **MARKETING AUTHORISATION NUMBER(S)**

EU/1/00/133/033 1 pen
EU/1/00/133/034 3 pens
EU/1/00/133/035 5 pens
EU/1/00/133/036 10 pens

13. **BATCH NUMBER**

Batch

14. **GENERAL CLASSIFICATION FOR SUPPLY**

15. **INSTRUCTIONS ON USE**

16. **INFORMATION IN BRAILLE**

Toujeo 300
MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PEN LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Toujeo 300 units/ml injection
insulin glargine
Subcutaneous use

2. METHOD OF ADMINISTRATION

Use only in this pen or severe overdose can result.

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1.5 ml

6. OTHER

SoloStar
PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (5 ml vial)

1. NAME OF THE MEDICINAL PRODUCT

Toujeo 100 units/ml solution for injection in a vial
Insulin glargine

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 ml contains 100 units (3.64 mg) insulin glargine

3. LIST OF EXCIPIENTS

Excipients: zinc chloride, metacresol, glycerol, hydrochloric acid (for pH adjustment), sodium hydroxide (for pH adjustment), water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
1 vial of 5 ml.
2 vials of 5 ml.
5 vials of 5 ml.
10 vials of 5 ml.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Use only clear and colourless solutions.

8. EXPIRY DATE

EXP
9. **SPECIAL STORAGE CONDITIONS**

Unopened vials:
Store in a refrigerator.
Do not freeze or place next to the freezer or freezer pack.

Once in use, vials may be stored for a maximum of 4 weeks not above 25°C.

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

10. **SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

11. **NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Sanofi-Aventis Deutschland GmbH
D-65926 Frankfurt am Main, Germany.

12. **MARKETING AUTHORISATION NUMBER(S)**

EU/1/00/133/001 1 vial of 5 ml
EU/1/00/133/002 2 vials of 5 ml
EU/1/00/133/003 5 vials of 5 ml
EU/1/00/133/004 10 vials of 5 ml

13. **BATCH NUMBER**

BN

14. **GENERAL CLASSIFICATION FOR SUPPLY**

Medicinal product subject to medical prescription.

15. **INSTRUCTIONS ON USE**

16. **INFORMATION IN BRAILLE**

Toujeo
MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL (5 ml vial)

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Toujeo 100 units/ml solution for injection
Insulin glargine

2. METHOD OF ADMINISTRATION

Subcutaneous use.

3. EXPIRY DATE

EXP
Date of first use: ............... 

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

5 ml

6. OTHER
PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (10 ml vial)

1. **NAME OF THE MEDICINAL PRODUCT**

   Toujeo 100 units/ml solution for injection in a vial
   Insulin glargine

2. **STATEMENT OF ACTIVE SUBSTANCE(S)**

   1 ml contains 100 units (3.64 mg) insulin glargine

3. **LIST OF EXCIPIENTS**

   Excipients: zinc chloride, metacresol, glycerol, hydrochloric acid (for pH adjustment), polysorbate 20, sodium hydroxide (for pH adjustment), water for injections

4. **PHARMACEUTICAL FORM AND CONTENTS**

   Solution for injection
   1 vial of 10 ml

5. **METHOD AND ROUTE(S) OF ADMINISTRATION**

   Read the package leaflet before use.
   Subcutaneous use.

6. **SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN**

   Keep out of the sight and reach of children.

7. **OTHER SPECIAL WARNING(S), IF NECESSARY**

   Use only clear and colourless solutions.

8. **EXPIRY DATE**

   EXP
9. SPECIAL STORAGE CONDITIONS

Unopened vials:
Store in a refrigerator.
Do not freeze or place next to the freezer or freezer pack.

Once in use, vials may be stored for a maximum of 4 weeks not above 30°C.

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

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Sanofi-Aventis Deutschland GmbH
D-65926 Frankfurt am Main, Germany.

12. MARKETING AUTHOURISATION NUMBER(S)

EU/1/00/133/008

13. BATCH NUMBER

BN

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Toujeo
MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS LABEL (10 ml vial)

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Toujeo 100 units/ml solution for injection
Insulin glargine

2. METHOD OF ADMINISTRATION

Subcutaneous use.

3. EXPIRY DATE

EXP
Date of first use: ……………

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

10 ml

6. OTHER
**PARTICULARS TO APPEAR ON THE OUTER PACKAGING**

**OUTER CARTON (cartridge)**

1. **NAME OF THE MEDICINAL PRODUCT**

   Toujeo 100 units/ml solution for injection in a cartridge
   Insulin glargine

2. **STATEMENT OF ACTIVE SUBSTANCE(S)**

   1 ml contains 100 units (3.64 mg) insulin glargine

3. **LIST OF EXCIPIENTS**

   Excipients: zinc chloride, metacresol, glycerol, hydrochloric acid (for pH adjustment), sodium hydroxide (for pH adjustment), water for injections

4. **PHARMACEUTICAL FORM AND CONTENTS**

   Solution for injection
   4 cartridges of 3 ml.
   5 cartridges of 3 ml.
   10 cartridges of 3 ml.

5. **METHOD AND ROUTE(S) OF ADMINISTRATION**

   The Toujeo cartridges are to be used only with the pens: OptiPen, ClikSTAR, Tactipen, Autopen 24, AllStar, JuniorSTAR.
   Nor all these pens may be marketed in your country.
   Read the package leaflet before use.
   Subcutaneous use.

6. **SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN**

   Keep out of the sight and reach of children.

7. **OTHER SPECIAL WARNING(S), IF NECESSARY**

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

8. **EXPIRY DATE**
9. SPECIAL STORAGE CONDITIONS

Unopened cartridges
Store in a refrigerator.
Do not freeze or place next to the freezer or a freezer pack. Keep the cartridge in the outer carton in order to protect from light.

Once in use the cartridge may be stored for a maximum of 4 weeks not above 30°C. The pen containing the cartridge must not be stored in the refrigerator.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Sanofi-Aventis Deutschland GmbH
D-65926 Frankfurt am Main, Germany.

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/00/133/005 4 cartridges of 3 ml
EU/1/00/133/006 5 cartridges of 3 ml
EU/1/00/133/007 10 cartridges of 3 ml

13. BATCH NUMBER

BN

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Toujeo
MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL (cartridge)

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Toujeo 100 units/ml solution for injection
Insulin glargine

2. METHOD OF ADMINISTRATION

Subcutaneous use.
Use specific pens: see leaflet.

3. EXPIRY DATE

EXP

4. BATCH NUMBER

BN

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3 ml

6. OTHER
MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

TEXT TO APPEAR ON THE ALUMINIUM FOIL WHICH IS USED FOR SEALING TRANSPARENT PLASTIC TRAY CONTAINING THE CARTRIDGE

1. NAME OF THE MEDICINAL PRODUCT

2. NAME OF THE MARKETING AUTHORISATION HOLDER

3. EXPIRY DATE

4. BATCH NUMBER

5. OTHER

After inserting a new cartridge:
You must check that your insulin pen is working properly before you inject the first dose. Consult your insulin pen instruction booklet for further details.
PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (cartridge for OptiClik)

1. NAME OF THE MEDICINAL PRODUCT

Toujeo 100 units/ml solution for injection in a cartridge for OptiClik
Insulin glargine

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 ml contains 100 units (3.64 mg) insulin glargine

3. LIST OF EXCIPIENTS

Excipients: zinc chloride, metacresol, glycerol, hydrochloric acid (for pH adjustment), sodium hydroxide (for pH adjustment), water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
1 cartridge of 3 ml.
3 cartridges of 3 ml.
4 cartridges of 3 ml.
5 cartridges of 3 ml.
6 cartridges of 3 ml.
8 cartridges of 3 ml.
9 cartridges of 3 ml.
10 cartridges of 3 ml.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

To be used with OptiClik only.
Read the package leaflet before use.
Subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Use only clear and colourless solutions.
If OptiClik is damaged or not working properly (due to mechanical defects) it has to be discarded, and a new OptiClik has to be used.
8.  EXPIRY DATE

EXP

9.  SPECIAL STORAGE CONDITIONS

Unopened cartridges:
Store in a refrigerator.
Do not freeze or place next to the freezer or a freezer pack. Keep the cartridge in the outer carton in order to protect from light.

Once in use the cartridge may be stored for a maximum of 4 weeks not above 30°C. The pen containing the cartridge must not be stored in the refrigerator.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Sanofi-Aventis Deutschland GmbH
D-65926 Frankfurt am Main, Germany.

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/00/133/017 1 cartridge of 3 ml
EU/1/00/133/018 3 cartridges of 3 ml
EU/1/00/133/019 4 cartridges of 3 ml
EU/1/00/133/020 5 cartridges of 3 ml
EU/1/00/133/021 6 cartridges of 3 ml
EU/1/00/133/022 8 cartridges of 3 ml
EU/1/00/133/023 9 cartridges of 3 ml
EU/1/00/133/024 10 cartridges of 3 ml

13. BATCH NUMBER

BN

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INFORMATION ON USE

16. INFORMATION IN BRAILLE

Toujeo OptiClik
MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL (cartridge for OptiClik)

<table>
<thead>
<tr>
<th>1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION</th>
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</thead>
<tbody>
<tr>
<td>Toujeo 100 units/ml solution for injection</td>
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<tr>
<td>Insulin glargine</td>
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</table>

<table>
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<tr>
<th>2. METHOD OF ADMINISTRATION</th>
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<tbody>
<tr>
<td>Subcutaneous use. To be used with OptiClik only.</td>
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<th>4. BATCH NUMBER</th>
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<td>Lot</td>
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<tr>
<th>5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT</th>
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<tbody>
<tr>
<td>3 ml</td>
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<table>
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<tr>
<th>6. OTHER</th>
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</thead>
</table>
PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (Pre-filled pen. OptiSet)

1. NAME OF THE MEDICINAL PRODUCT

Toujeo OptiSet 100 units/ml solution for injection in a pre-filled pen.
Insulin glargine

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 ml contains 100 units (3.64 mg) insulin glargine

3. LIST OF EXCIPIENTS

Excipients: zinc chloride, metacresol, glycerol, hydrochloric acid (for pH adjustment), sodium hydroxide (for pH adjustment), water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
1 pen of 3 ml
3 pens of 3 ml
4 pens of 3 ml
5 pens of 3 ml
6 pens of 3 ml
8 pens of 3 ml
9 pens of 3 ml
10 pens of 3 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.
7. OTHER SPECIAL WARNING(S), IF NECESSARY

Use only clear and colourless solutions.
Only use needles that are compatible for use with OptiSet.

IMPORTANT INFORMATION
Always first attach a new needle before using OptiSet.
Always perform a safety test before using OptiSet.
Read the package leaflet fully before using OptiSet for the first time

Information for use:
• Name of the insulin is printed on the pen
• Dosage selector can only be turned in one direction

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Not in-use pens:
Store in a refrigerator.
Do not freeze or place next to the freezer or a freezer pack. Keep the pre-filled pen in the outer carton in order to protect from light.

Once in use the pens may be stored for a maximum of 4 weeks not above 30°C. When in use, the pen must not be stored in the refrigerator.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Sanofi-Aventis Deutschland GmbH
D-65926 Frankfurt am Main, Germany.

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/00/133/009 1 pen of 3 ml
EU/1/00/133/010 3 pens of 3 ml
EU/1/00/133/011 4 pens of 3 ml
EU/1/00/133/012 5 pens of 3 ml
EU/1/00/133/013 6 pens of 3 ml
EU/1/00/133/014 8 pens of 3 ml
EU/1/00/133/015 9 pens of 3 ml
EU/1/00/133/016 10 pens of 3 ml
13. **BATCH NUMBER**

BN

14. **GENERAL CLASSIFICATION FOR SUPPLY**

Medicinal product subject to medical prescription.

15. **INSTRUCTIONS ON USE**

16. **INFORMATION IN BRAILLE**

Toujeo OptiSet
MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PEN LABEL (Pre-filled pen. OptiSet)

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Toujeo OptiSet 100 units/ml solution for injection
Insulin glargine
Subcutaneous use.

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3 ml

6. OTHER
PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (Pre-filled pen. SoloStar)

1. NAME OF THE MEDICINAL PRODUCT

Toujeo SoloStar 100 units/ml solution for injection in a pre-filled pen
Insulin glargine

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 ml contains 100 units (3.64 mg) insulin glargine

3. LIST OF EXCIPIENTS

Excipients: zinc chloride, metacresol, glycerol, hydrochloric acid (for PH adjustment), sodium hydroxide (for PH adjustment), water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
1 pen of 3 ml.
3 pens of 3 ml.
4 pens of 3 ml.
5 pens of 3 ml.
6 pens of 3 ml.
8 pens of 3 ml.
9 pens of 3 ml.
10 pens of 3 ml.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use.
Open here

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Use only clear and colourless solutions.
Only use needles that are compatible for use with SoloStar.
8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Unopened
Store in a refrigerator. Do not freeze or place next to the freezer or a freezer pack. Keep the pre-filled pen in the outer carton in order to protect from light.

In use conditions
After its first use, the pen may be stored for a maximum of 4 weeks not above 30°C. Do not refrigerate. Keep the pen protected from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Sanofi-Aventis Deutschland GmbH
D-65926 Frankfurt am Main, Germany.

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/00/133/025 1 pen of 3 ml.
EU/1/00/133/026 3 pens of 3 ml.
EU/1/00/133/027 4 pens of 3 ml.
EU/1/00/133/028 5 pens of 3 ml.
EU/1/00/133/029 6 pens of 3 ml.
EU/1/00/133/030 8 pens of 3 ml.
EU/1/00/133/031 9 pens of 3 ml.
EU/1/00/133/032 10 pens of 3 ml.

13. BATCH NUMBER

BN

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Toujeo SoloStar
<table>
<thead>
<tr>
<th>MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS</th>
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<tbody>
<tr>
<td>PEN LABEL (Pre-filled pen. SoloStar)</td>
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<table>
<thead>
<tr>
<th>1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION</th>
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<tbody>
<tr>
<td>Toujeo SoloStar 100 units/ml solution for injection.</td>
</tr>
<tr>
<td>Insulin glargine</td>
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<tr>
<td>Subcutaneous use</td>
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<tr>
<th>2. METHOD OF ADMINISTRATION</th>
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<tr>
<td>3 ml</td>
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<tr>
<th>6. OTHER</th>
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</table>
B. PACKAGE LEAFLET
Package leaflet: information for the user

Toujeo 300 units/ml solution for injection in a pre-filled pen
Insulin glargine

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet
1. What Toujeo is and what it is used for
2. What you need to know before you use Toujeo
3. How to use Toujeo
4. Possible side effects
5. How to store Toujeo
6. Contents of the pack and other information

1. What Toujeo is and what it is used for

Toujeo contains insulin called “insulin glargine”. This is a modified insulin, very similar to human insulin.

Toujeo contains 3 times more insulin in 1 ml than standard insulin, which contains 100 unit/ml.

It is used to treat diabetes mellitus in adults. Diabetes mellitus is an illness where your body does not make enough insulin to control your blood sugar.

Toujeo lowers your blood sugar steadily over a long period of time. It is used for once daily dosing. You can change the time of your injection if you need to. This is because this medicine lowers your blood sugar over a long period of time (for more information, see section 3).

2. What you need to know before you use Toujeo

Do not use Toujeo
- If you are allergic to insulin glargine or to any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor, pharmacist or nurse before using Toujeo.

Follow closely the instructions for dose, monitoring (blood and urine tests), diet and physical activity (physical work and exercise) and injection technique, as discussed with your doctor.
Be especially aware of the following:

- Too low blood sugar (hypoglycaemia). If your blood sugar is too low, follow the guidance for hypoglycaemia (see information in the box at the end of this leaflet).
- If you switch from another type, brand or manufacturer of insulin your insulin dose may need to be changed.
- Pioglitazone. See “Pioglitazone used together with insulin”.
- Ensure to use the right insulin. Medication errors due to mix-up between insulins, particularly between long-acting insulins and rapid-acting insulins have been reported. You must always check the insulin label before each injection to avoid mix-ups between Toujeo and other insulins.
- Never use a syringe to remove Toujeo from your SoloStar pre-filled pen. This is to avoid dosing errors and potential overdose which may lead to low blood sugar. Please, see also section 3.
- If you are blind or have poor eye sight, do not use the pre-filled pen without help. This is because you will not be able to read the dose window on the pen. Get help from a person with good eye sight who is trained in using the pen. If you have poor eyesight, please see section 3.

Illnesses and injuries
In the following situations, the management of your diabetes may require extra care (for example, blood and urine tests):

- If you are ill or have a major injury. Your blood sugar level may increase (hyperglycaemia).
- If you are not eating enough. Your blood sugar level may become too low (hypoglycaemia).

In most cases you will talk to a doctor. Contact a doctor as soon as you feel ill or get an injury.

If you have “Type 1” diabetes and you have an illness or injury:
- Do not stop your insulin
- Keep eating enough carbohydrates.

Always tell people who are caring or treating you, that you have diabetes.

Insulin treatment can cause the body to produce antibodies to insulin (substances that act against insulin). However, only very rarely, this will require a change to your insulin dose.

Travel
Talk to your doctor before travelling. You may need to talk about:

- If your type of insulin is available in the country you are visiting.
- How to arrange the supply of insulin, needles and other items.
- How to correctly store your insulin while travelling.
- The time you eat meals and use your insulin.
- The possible effects of changing to different time zones.
- Any health risks in the countries you will visit.
- What you should do in an emergency situation if you feel unwell or become ill.

Children and adolescents
This medicine should not be used in children or adolescents under 18 years of age. This is because there is no experience with Toujeo in this age group.

Other medicines and Toujeo
Tell your doctor, pharmacist or nurse if you are taking, have recently taken or might take any other medicines.

Some medicines can change your blood sugar level. This may mean your insulin dose has to change. So, before taking a medicine ask your doctor if it will affect your blood sugar and what action, if any, you need to take. You also need to be careful when you stop taking a medicine.

Your blood sugar level may fall (hypoglycaemia) if you take:

- Any other medicine to treat diabetes.
- Disopyramide – for some heart problems.
• Fluoxetine – for depression.
• Sulfonamide antibiotics.
• Fibrates – for lowering high levels of blood fats.
• Monoamine oxidase inhibitors (MAOIs) – for depression.
• Angiotensin converting enzyme (ACE) inhibitors – for heart problems or high blood pressure.
• Medicines to relieve pain and lower fever, such as pentoxifylline, propoxyphene and salicylates (such as acetylsalicylic acid).
• Pentamidine – for some infections caused by parasites. This may cause too low blood sugar which is sometimes followed by too high blood sugar.

Your blood sugar level may rise (hyperglycaemia) if you take:
• Corticosteroids such as cortisone – for inflammation.
• Danazol – for endometriosis.
• Diazoxide – for high blood pressure.
• Protease inhibitors- for HIV.
• Diuretics – for high blood pressure or fluid retention.
• Glucagon – for very low blood sugar.
• Isoniazid – for tuberculosis.
• Somatropin – a growth hormone.
• Thyroid hormones – for thyroid gland problems.
• Oestrogens and progestogens – such as in the contraceptive pill for birth control.
• Clozapine, olanzapine and phenothiazine derivatives – for mental health problems.
• Sympathomimetic medicines such as epinephrine (adrenaline), salbutamol and terbutaline – for asthma.

Your blood sugar level may either rise or fall if you take:
• Beta-blockers or clonidine – for high blood pressure.
• Lithium salts – for mental health problems.

**Beta-blockers**
Beta-blockers like other “Sympatholytic medicines” (such as clonidine, guanethidine, reserpine – for high blood pressure) may make it harder to recognise warning signs of your blood sugar being too low (hypoglycaemia). It can even hide or stop the first signs that your blood sugar is too low.

**Pioglitazone used together with insulin**
Some patients with long-standing type 2 diabetes mellitus and heart disease or previous stroke who were treated with pioglitazone and insulin experienced the development of heart failure. If you experience signs of heart failure such as unusual shortness of breath, a rapid increase in weight or localised swelling (oedema). Inform your doctor as soon as possible.

If any of the above apply to you (or you are not sure), talk to your doctor, pharmacist or nurse before using Toujeo.

**Toujeo with alcohol**
Your blood sugar level may either rise or fall if you drink alcohol. You should check your blood sugar level more than usual.

**Pregnancy and breast-feeding**
If you are pregnant or breast-feeding, think you might be pregnant or are planning to have a baby, ask your doctor for advice before using this medicine. Your insulin dose may need to be changed during pregnancy and after giving birth. For the health of your baby, it is particularly important to carefully control your diabetes and to prevent hypoglycaemia.
If you are breast-feeding, talk to your doctor, as your insulin doses and your diet might need to be changed.
Driving and using machines
Having too low or too high blood sugar or sight problems can affect your ability to drive and use tools or machines. Your concentration may be affected. This could be dangerous to yourself and others.

Ask your doctor whether you can drive if:
- Your blood sugar is often too low.
- You find it hard to recognise when your blood sugar is too low.

Important information about some of the ingredients of Toujeo
This medicine contains less than 1 mmol (23 mg) sodium per dose. This means it is essentially ‘sodium-free’.

3. How to use Toujeo

Always use this medicine exactly as your doctor has told you. Check with your doctor, pharmacist or nurse if you are not sure.

Although Toujeo contains the same active substance as insulin glargine 100 units/ml, these medicines are not interchangeable. The switch from one insulin therapy to another requires medical prescription, medical supervision and blood glucose monitoring. Please, consult your doctor for further information.

How much to use
The Toujeo SoloStar pre-filled pen can provide a dose of 1 to 80 units in one injection, in steps of 1 unit.
The dose window of the SoloStar pen shows the number of units of Toujeo to be injected. Do not make any dose re-calculation.

Based on your lifestyle, your blood sugar tests and your previous insulin use, your doctor will tell you:
- How much Toujeo you need each day and at what time.
- When to check your blood sugar level and if you need to carry out urine tests.
- When you may need a higher or lower dose.

Toujeo is a long-acting insulin. Your doctor may tell you to use it with a short-acting insulin, or with other medicines for high blood sugar.

If you use more than one insulin always ensure you use the right insulin by checking the insulin label before each injection. Medication errors due to mix-up between insulins, particularly between long-acting insulins and rapid-acting insulins have been reported. The strength “300” is highlighted in honey gold on the label of your Toujeo SoloStar pre-filled pen. Ask your doctor or pharmacist if you are not sure.

Many factors may affect your blood sugar level. You should know these factors so that you can take the right action if your blood sugar level changes and help step it becoming too high or too low. See the box at the end of this leaflet for more information.

Flexibility in time of administration
- Use Toujeo once a day, preferably at the same time every day.
- When needed, you can inject it up to 3 hours before or after the usual time that you use it.

Use in elderly patients (65 years and over)
If you are 65 years or older, talk to your doctor as you may need a lower dose.

If you have kidney or liver problems
If you have kidney or liver problems, talk to your doctor as you may need a lower dose.
Before injecting Toujeo
• Read the instructions for use that come with this package leaflet.
• If you do not follow all of these instructions, you may get too much or too little insulin.

How to inject
• Toujeo is injected under the skin (subcutaneous use or “SC”).
• Inject it into the front of your thighs, upper arms or the front of your waist (abdomen).
• Change the place within the area you inject each day. This will reduce the risk of skin shrinking or thickening (for more information, see “Other side effects” in section 4).

To prevent the possible transmission of disease, insulin pens should never be used for more than one person, even when the needle is changed.

Always attach a new sterile needle before each injection. Never re-use needles. If you re-use a needle this increases the risk of it becoming blocked and of you getting too much or too little insulin.

Throw away the used needle in a puncture resistant container, or as told by your pharmacist or local authority.

Do not use Toujeo
• In a vein. This will change the way it works and may cause your blood sugar to become too low.
• In an insulin infusion pump.
• If there are particles in the insulin. The solution should be clear, colourless and water-like.

Never use a syringe to remove Toujeo from your SoloStar pen or severe overdose can result. Please, see also section 2.

If the SoloStar pen is damaged, has not been stored correctly, if you are not sure that it is working properly or you notice that your blood sugar control is unexpectedly getting worse:
• Throw the pen away and use a new one.
• Talk to your doctor, pharmacist or nurse if you think you have problem with your pen.

If you use more Toujeo than you should
If you have injected too much of this medicine, your blood sugar level may become too low. Check your blood sugar and eat more food to prevent you blood sugar getting too low. If your blood sugar gets too low, see the advice in the box at the end of this leaflet.

If you forget to use Toujeo
When needed, Toujeo can be injected up to 3 hours before or after the time you usually inject it.

If you have missed a dose of Toujeo or if you have not injected enough insulin, your blood sugar level may become too high (hyperglycaemia):
• Do not inject a double dose to make up for a forgotten dose.
• Check your blood sugar and then inject your next dose at the usual time.
• For information on the treatment of hyperglycaemia, see the box at the end of this leaflet.

If you stop using Toujeo
Do not stop using this medicine without talking to your doctor. If you do, it could lead to very high blood sugar and a build-up of acid in the blood (ketoacidosis).

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects
Like all medicines, this medicine can cause side effects, although not everybody gets them.
If you notice signs of your blood sugar being too low (hypoglycaemia), take action to increase your blood sugar level straight away (see the box at the end of this leaflet). Hypoglycaemia can be very serious and is very common with insulin treatment (may affect more than 1 in 10 people).

Low blood sugar means that there is not enough sugar in your blood.
If your blood sugar falls too low, you may pass out (become unconscious).
Serious low blood sugar may cause brain damage and may be life-threatening.
For more information, see the box at the end of this leaflet.

Severe allergic reactions (rare, may affect up to 1 in 1,000 people). The signs may include rash and itching all over the body, swelling of skin or mouth, shortness of breath, feeling faint (a fall in blood pressure) with fast heart beat and sweating. Severe allergic reactions may become life-threatening.
Tell a doctor straight away if you notice signs of a severe allergic reaction.

Other side effects
Tell your doctor, pharmacist or nurse if you notice any of the following side effects:

Common: may affect up to 1 in 10 people
- Skin changes where the injection is given: If you inject insulin too often at the same place, the skin may either shrink (lipoatrophy) or thicken (lipohypertrophy). The insulin may not work very well. Change the injection site with each injection to help prevent these skin changes.
- Skin and allergic reactions at the injection site: The signs may include reddening, unusually intense pain when injecting, itching, hives, swelling or inflammation. This can spread around the injection site. Most minor reactions to insulins usually disappear in a few days to a few weeks.

Rare: may affect up to 1 in 1,000 people
- Eye reactions: A big change in your blood sugar control (getting better or worse) can disturb your vision. If you have an eye disorder related to diabetes called “proliferative retinopathy”, very low blood sugar attack may cause temporary loss of vision.
- Swelling in the calves and ankles, caused by temporary build-up of water in the body.

Very rare: may affect up to 1 in 10,000 people
- Changes in taste (dysgeusia).
- Muscular pain (myalgia).

Tell your doctor, pharmacist or nurse if you notice any of the side effects above.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Toujeo

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and on the label of the pen after “EXP”. The expiry date refers to the last day of that month.

Before first use
Store in a refrigerator (2°C-8°C).
Do not freeze or place next to the freezer compartment or a freezer pack.
Keep the pen in the outer carton in order to protect from light.
After first use or if carried as a spare
Do not store the pen in a refrigerator. The pen may be stored for a maximum of 6 weeks below 30°C and away from direct heat or direct light. Discard the pen after this time period. Do not leave your insulin in a car on an exceptionally warm or cold day. Always keep the cap on the pen when you are not using it in order to protect from light.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer used. These measures will help protect the environment.

6. Contents of the pack and other information

What Toujeo contains
- The active substance is insulin glargine. Each ml of the solution contains 300 units of insulin glargine (equivalent to 10.91 mg). Each pen contains 1.5 ml of solution for injection, equivalent to 450 units.
- The other ingredients are: zinc chloride, metacresol, glycerol, water for injections, and sodium hydroxide (see section 2 “Important information about some of the ingredients of Toujeo”) and hydrochloric acid (for pH adjustment).

What Toujeo looks like and contents of the pack
Toujeo is a clear and colourless solution. Each pen contains 1.5 ml of solution for injection (equivalent to 450 units). Packs of 1, 3, 5 and 10 pre-filled pens. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
Sanofi-Aventis Deutschland GmbH, D-65926 Frankfurt am Main, Germany.

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder.

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Other source of information
Detailed information on this medicine is available on the European Medicines Agency web site:
http://www.ema.europa.eu/
HYPERGLYCAEMIA AND HYPOGLYCAEMIA

If you take insulin, you should always carry the following things with you:

- Sugar (at least 20 grams).
- Information so that others know you have diabetes.

Hyperglycaemia (high blood sugar levels)

If your blood sugar is too high (hyperglycaemia), you may not have injected enough insulin.

Reasons why hyperglycaemia may happen:

Examples include:

- You have not injected your insulin or not injected enough.
- Your insulin has become less effective – for example because it was not stored properly.
- Your insulin pen does not work properly.
- You are doing less exercise than usual.
- You are under stress – such as emotional distress or excitement.
- You have an injury, infection or fever or have had an operation.
- You are taking or have taken certain other medicines (see section 2, "Other medicines and Toujeo").

Warning signs of hyperglycaemia
Thirst, increased need to urinate, tiredness, dry skin, reddening of the face, loss of appetite, low blood pressure, fast heart beat, and glucose and ketone bodies in urine. Stomach pain, fast and deep breathing, feeling sleepy or passing out (becoming unconscious) may be signs of a serious condition (ketoacidosis) resulting from lack of insulin.

What to do if you experience hyperglycaemia

- Test your blood sugar level and your urine for ketones as soon as you notice any of the above signs
- Contact your doctor straight away if you have severe hyperglycaemia or ketoacidosis. This must always be treated by a doctor, normally in a hospital.

Hypoglycaemia (low blood sugar levels)

If your blood sugar level falls too much you may pass out (become unconscious). Serious hypoglycaemia may cause a heart attack or brain damage and may be life-threatening. You should learn to recognise the signs when your blood sugar is falling – so you can take action to stop it getting worse.

Reasons why hypoglycaemia may happen:

Examples include:

- You inject too much insulin.
- You miss meals or delay them.
- You do not eat enough, or eat food containing less sugar (carbohydrate) than normal – artificial sweeteners are not carbohydrates.
- You drink alcohol – especially when you have not eaten much.
- You lose carbohydrates from being sick (vomiting) or diarrhoea.
- You are doing more exercise than usual or a different type of physical activity.
- You are recovering from an injury, operation or other stress.
- You are recovering from an illness or from fever.
- You are taking or have stopped taking certain other medicines (see section 2, "Other medicines and Toujeo").
Hypoglycaemia is also more likely to happen if:
- You have just started insulin treatment or changed to another insulin – if low blood sugar occurs, it may be more likely to happen in the morning.
- Your blood sugar levels are almost normal or are unstable.
- You change the area of skin where you inject insulin. For example from the thigh to the upper arm.
- You have severe kidney or liver disease, or some other disease such as hypothyroidism.

Warning signs of hypoglycaemia
The first signs may be in your body generally. Examples of signs that your blood sugar level is falling too much or too fast include: sweating, clammy skin, feeling anxious, fast or irregular heart beat, high blood pressure and palpitations. These signs often develop before the signs of a low sugar level in the brain.

Signs in your brain include: headaches, feeling very hungry, feeling sick (nausea) or being sick (vomiting), feeling tired, sleepy, restless, sleeping problems, aggressive behaviour, difficulty concentrating, slow reactions, depression, feeling confused, difficulty speaking (sometimes total loss of speech), changes in your sight, trembling, being unable to move (paralysis), tingling in the hands or arms, feeling numb and tingling often around the mouth, feeling dizzy, loss of self-control, being unable to look after yourself, fits, passing out.

When the signs of hypoglycaemia may be less clear:
The first warning signs of hypoglycaemia may change, be weaker or missing altogether if:
- You are elderly.
- You have had diabetes for a long time.
- You have a certain type of nervous disease (called “diabetic autonomic neuropathy”).
- You have recently had too low blood sugar (for example the day before).
- Your low blood sugar comes on slowly.
- Your low blood sugar is always around “normal” or your blood sugar has got much better.
- You have recently changed from an animal insulin to a human insulin, like Toujeo.
- You are taking or have taken certain other medicines (see section 2, "Other medicines and Toujeo").

In such cases, you may develop severe hypoglycaemia (and even pass out) before you know what is happening. Be familiar with your warning signs. If necessary, you might need to test your blood sugar more often. This can help to spot mild hypoglycaemic episodes. If you find it difficult to recognise your warning signs, you should avoid situations (such as driving a car) in which you or others would be put at risk by hypoglycaemia.

What to do if you experience hypoglycaemia?
1. Do not inject insulin. Take about 10 to 20 grams sugar straight away - such as glucose, sugar cubes or a sugary-drink. Do not drink or eat foods that contain artificial sweeteners (such as diet drinks). They do not help treat low blood sugar.
2. Then eat something (such as bread or pasta) that will raise your blood sugar over a longer time. Ask your doctor or nurse if you are not sure which foods you should eat. With Toujeo, it may take longer to recover from low blood sugar because it is long-acting.
3. If the hypoglycaemia comes back again, take another 10 to 20 grams of sugar.
4. Speak to a doctor straight away if you are not able to control the hypoglycaemia, or it comes back again.

What other people should do if you have hypoglycaemia
Tell your relatives, friends and close colleagues to get medical help straight away if you are not able to swallow or if you pass out (become unconscious).
You will require an injection of glucose or glucagon (a medicine which increases blood sugar). These injections should be given even if it is not certain that you have hypoglycaemia.

You should test your blood sugar straight away after taking glucose to check that you really have hypoglycaemia.
**Toujeo 300 units/ml solution for injection in a pre-filled pen (SoloStar)**

**INSTRUCTIONS FOR USE**

**Read this first**

**Toujeo SoloStar contains 300 units/ml insulin glargine** in a 1.5 ml disposable prefilled pen

- **Never re-use needles.** If you do you might not get your dose (underdosing) or get too much (overdosing) as the needle could block.
- **Never use a syringe to remove insulin from your pen.** If you do you will get too much insulin. The scale on most syringes is made for non-concentrated insulin only.

**Important information**

- **Never share your pen – it is only for you.**
- **Never use your pen if it is damaged or if you are not sure that it is working properly.**
- **Always perform a safety test**
- **Always carry a spare pen and spare needles in case they got lost or stop working.**

**Learn to inject**

- Talk with your doctor, pharmacist or nurse about how to inject, before using your pen.
- Ask for help if you have problems handling the pen, for example if you have problems with your sight.
- Read all of these instructions before using your pen. If you do not follow all of these instructions, you may get too much or too little insulin.

**Need help?**

If you have any questions about your pen or about diabetes, ask your doctor, pharmacist or nurse or call sanofi-aventis number on the front of this leaflet.

**Extra items you will need:**

- a new sterile needle (see STEP 2).
- a puncture resistant container for used needles and pens.

**Places to inject**

- Upper arms
- Stomach
- Thighs
Get to know your pen

STEP 1: Check your pen

Take a new pen out of the fridge at least 1 hour before you inject. Cold insulin is more painful to inject.

A Check the name and expiration date on the label of your pen.
- Make sure you have the correct insulin. This is especially important if you have other injector pens.
- Never use your pen after the expiration date.

B Pull off the pen cap.

C Check that the insulin is clear.
- Do not use the pen if the insulin looks cloudy, coloured or contains particles.

STEP 2: Attach a new needle

Always use a new sterile needle for each injection. This helps stop blocked needles, contamination and infection.
Only use needles that are compatible for use with Toujeo (e.g. needles from BD, Ypsomed, Artsana or Owen Mumford).

A  Take a new needle and peel off the protective seal.

B  Keep the needle straight and screw it onto the pen until fixed. Do not overtighten.

C  Pull off the outer needle cap. Keep this for later.

D  Pull off the inner needle cap and throw away.

Handling needles
- Take care when handling needles – this is to prevent needle injury and cross-infection.
STEP 3: Do a safety test

Always do a safety test before each injection – this is to:
• check your pen and the needle are working properly.
• make sure that you get the correct insulin dose.

A Select 3 units by turning the dose selector until the dose pointer is at the mark between 2 and 4.

B Press the injection button all the way in.
• When insulin comes out of the needle tip, your pen is working correctly.

If no insulin appears:
• You may need to repeat this step up to 3 times before seeing insulin.
• If no insulin comes out after the third time, the needle may be blocked. If this happens:
  - change the needle (see STEP 6 and STEP 2),
  - then repeat the safety test (STEP 3).
• Do not use your pen if there is still no insulin coming out of the needle tip. Use a new pen.
• Never use a syringe to remove insulin from your pen.

If you see air bubbles
• You may see air bubbles in the insulin. This is normal, they will not harm you.

STEP 4: Select the dose

Never select a dose or press the injection button without a needle attached. This may damage your pen.
A  Make sure a needle is attached and the dose is set to ‘0’.

B  Turn the dose selector until the dose pointer lines up with your dose.
   • If you turn past your dose, you can turn back down.
   • If there are not enough units left in your pen for your dose, the dose selector will stop at the
     number of units left.
   • If you cannot select your full prescribed dose, split the dose into two injections or use a new
     pen.

How to read the dose window

Even numbers are shown in line with the dose pointer:

Odd numbers are shown as a line between even numbers:

Units of insulin in your pen

• Your pen contains a total of 450 units of insulin. You can select doses from 1 to 80 units in
  steps of 1 unit. Each pen contains more than one dose.
• You can see roughly how many units of insulin are left by looking at where the plunger is on
  the insulin scale.

STEP 5: Inject your dose

If you find it hard to press the injection button in, do not force it as this may break your pen. See
the section below for help.
A Choose a place to inject as shown in the picture

B Push the needle into your skin as shown by your doctor, pharmacist or nurse.
   • Do not touch the injection button yet.

C Place your thumb on the injection button. Then press all the way in and hold.
   • Do not press at an angle – your thumb could block the dose selector from turning.

D Keep the injection button held in and when you see "0" in the dose window, slowly count to 5.
   • This will make sure you get your full dose.

E After holding and slowly counting to 5, release the injection button. Then remove the needle from your skin.

1 If you find it hard to press the button in:
   • Change the needle (see STEP 6 and STEP 2) then do a safety test (see STEP 3).
   • If you still find it hard to press in, get a new pen.
   • Never use a syringe to remove insulin from your pen.

STEP 6: Remove the needle

✓ Take care when handling needles – this is to prevent needle injury and cross-infection.
✗ Never put the inner needle cap back on.

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, or if you are giving an injection to another person, special caution must be taken by this person when removing and disposing of the needle.

Follow recommended safety measures for removal and disposal of needles (contact your doctor, pharmacist or nurse) in order to reduce the risk of accidental needle injury and transmission of infectious diseases.

B Throw away the used needle in a puncture resistant container, or as told by your pharmacist or local authority.

C Put the pen cap back on.
- Do not put the pen back in the fridge.

Use by
- Only use your pen for up to 6 weeks after its first use.

How to store your pen

Before first use
- Keep new pens in a fridge, at 2°C to 8°C.
- Do not freeze.

After first use
- Keep your pen at room temperature, below 30°C.
- Never put your pen back in the fridge.
- Never store your pen with the needle attached.
- Store your pen with the pen cap on.

How to care for your pen

Handle your pen with care
- Do not drop your pen or knock it against hard surfaces.
- If you think that your pen may be damaged, do not try to repair it, use a new one.

Protect your pen from dust and dirt
- You can clean the outside of your pen by wiping it with a damp cloth. Do not soak, wash or lubricate your pen – this may damage it.
Throwing your pen away

- Remove the needle before throwing your pen away.
- Throw away your used pen as told by your pharmacist or local authority.
Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet
1. What Toujeo is and what it is used for
2. What you need to know before you use Toujeo
3. How to use Toujeo
4. Possible side effects
5. How to store Toujeo
6. Contents of the pack and other information

1. What Toujeo is and what it is used for

Toujeo contains insulin glargine. This is a modified insulin, very similar to human insulin.

Toujeo is used to treat diabetes mellitus in adults, adolescents and children aged 2 years and above. Diabetes mellitus is a disease where your body does not produce enough insulin to control the level of blood sugar. Insulin glargine has a long and steady blood-sugar-lowering action.

2. What you need to know before you use Toujeo

Do not use Toujeo

- If you are allergic to insulin glargine or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Toujeo. Follow closely the instructions for posology, monitoring (blood and urine tests), diet and physical activity (physical work and exercise) as discussed with your doctor.

If your blood sugar is too low (hypoglycaemia), follow the guidance for hypoglycaemia (see box at the end of this leaflet).

Travel

Before travelling consult your doctor. You may need to talk about
- the availability of your insulin in the country you are visiting,
- supplies of insulin, syringes etc.,
- correct storage of your insulin while travelling,
- timing of meals and insulin administration while travelling,
- the possible effects of changing to different time zones,
Illnesses and injuries

In the following situations, the management of your diabetes may require a lot of care (for example, adjustment to insulin dose, blood and urine tests):
- If you are ill or have a major injury then your blood sugar level may increase (hyperglycaemia).
- If you are not eating enough your blood sugar level may become too low (hypoglycaemia).
In most cases you will need a doctor. **Make sure that you contact a doctor early.**

If you have type 1 diabetes (insulin dependent diabetes mellitus), do not stop your insulin and continue to get enough carbohydrates. Always tell people who are caring for you or treating you that you require insulin.

Insulin treatment can cause the body to produce antibodies to insulin (substances that act against insulin). However, only very rarely, this will require a change to your insulin dose.

Some patients with long-standing type 2 diabetes mellitus and heart disease or previous stroke who were treated with pioglitazone (oral anti-diabetic medicine used to treat type 2 diabetes mellitus) and insulin experienced the development of heart failure. Inform your doctor as soon as possible if you experience signs of heart failure such as unusual shortness of breath or rapid increase in weight or localised swelling (oedema).

**Children**

There is no experience with the use of Toujeo in children below the age of 2 years.

**Other medicines and Toujeo**

Some medicines cause changes in the blood sugar level (decrease, increase or both depending on the situation). In each case, it may be necessary to adjust your insulin dose to avoid blood sugar levels that are either too low or too high. Be careful when you start or stop taking another medicine.

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. Before taking a medicine ask your doctor if it can affect your blood sugar level and what action, if any, you need to take.

**Medicines that may cause your blood sugar level to fall (hypoglycaemia) include:**
- all other medicines to treat diabetes,
- angiotensin converting enzyme (ACE) inhibitors (used to treat certain heart conditions or high blood pressure),
- disopyramide (used to treat certain heart conditions),
- fluoxetine (used to treat depression),
- fibrates (used to lower high levels of blood lipids),
- monoamine oxidase (MAO) inhibitors (used to treat depression),
- pentoxifylline, propoxyphene, salicylates (such as acetylsalicylic acid, used to relieve pain and lower fever),
- sulfonamide antibiotics.

**Medicines that may cause your blood sugar level to rise (hyperglycaemia) include:**
- corticosteroids (such as "cortisone" used to treat inflammation),
- danazol (medicine acting on ovulation),
- diazoxide (used to treat high blood pressure),
- diuretics (used to treat high blood pressure or excessive fluid retention),
- glucagon (pancreas hormone used to treat severe hypoglycaemia),
- isoniazid (used to treat tuberculosis),
- oestrogens and progestogens (such as in the contraceptive pill used for birth control),
- phenothiazine derivatives (used to treat psychiatric disorders),
- somatropin (growth hormone),
- sympathomimetic medicines (such as epinephrine [adrenaline], salbutamol, terbutaline used to treat asthma),
- thyroid hormones (used to treat thyroid gland disorders),
- atypical antipsychotic medicines (such as clozapine, olanzapine),
- protease inhibitors (used to treat HIV).

Your blood sugar level may either rise or fall if you take:
- beta-blockers (used to treat high blood pressure),
- clonidine (used to treat high blood pressure),
- lithium salts (used to treat psychiatric disorders).

Pentamidine (used to treat some infections caused by parasites) may cause hypoglycaemia which may sometimes be followed by hyperglycaemia.

Beta-blockers like other sympatholytic medicines (such as clonidine, guanethidine, and reserpine) may weaken or suppress entirely the first warning symptoms which help you to recognise a hypoglycaemia.

If you are not sure whether you are taking one of those medicines ask your doctor or pharmacist.

Toujeo with alcohol

Your blood sugar levels may either rise or fall if you drink alcohol.

Pregnancy and breast-feeding

Ask your doctor or pharmacist for advice before taking any medicine.

Inform your doctor if you are planning to become pregnant, or if you are already pregnant. Your insulin dose may need to be changed during pregnancy and after giving birth. Particularly careful control of your diabetes, and prevention of hypoglycaemia, is important for the health of your baby.

If you are breast-feeding consult your doctor as you may require adjustments in your insulin doses and your diet.

Driving and using machines

Your ability to concentrate or react may be reduced if:
- you have hypoglycaemia (low blood sugar levels),
- you have hyperglycaemia (high blood sugar levels),
- you have problems with your sight.

Keep this possible problem in mind in all situations where you might put yourself and others at risk (such as driving a car or using machines). You should contact your doctor for advice on driving if:
- you have frequent episodes of hypoglycaemia,
- the first warning symptoms which help you to recognise hypoglycaemia are reduced or absent.

Important information about some of the ingredients of Toujeo

This medicine contains less than 1 mmol (23 mg) sodium per dose, i.e. it is essentially ‘sodium-free’. 
3. **How to use Toujeo**

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

**Dose**

Based on your life-style and the results of your blood sugar (glucose) tests and your previous insulin usage, your doctor will:
- determine how much Toujeo per day you will need and at what time,
- tell you when to check your blood sugar level, and whether you need to carry out urine tests,
- tell you when you may need to inject a higher or lower dose of Toujeo.

Toujeo is a long-acting insulin. Your doctor may tell you to use it in combination with a short-acting insulin or with tablets used to treat high blood sugar levels.

Many factors may influence your blood sugar level. You should know these factors so that you are able to react correctly to changes in your blood sugar level and to prevent it from becoming too high or too low. See the box at the end of this leaflet for further information.

**Use in children and adolescents**

Toujeo can be used in adolescents and children aged 2 years and above. Use this medicine exactly as your doctor has told you.

**Frequency of administration**

You need one injection of Toujeo every day, at the same time of the day.

**Method of administration**

Toujeo is injected under the skin. Do NOT inject Toujeo in a vein, since this will change its action and may cause hypoglycaemia.

Your doctor will show you in which area of the skin you should inject Toujeo. With each injection, change the puncture site within the particular area of skin that you are using.

**How to handle the vials**

Look at the vial before you use it. Only use it if the solution is clear, colourless and waterlike, and has no visible particles in it. Do not shake or mix it before use. Make sure that neither alcohol nor other disinfectants or other substances contaminate the insulin. Do not mix Toujeo with any other insulins or medicines. Do not dilute it. Mixing or diluting may change the action of Toujeo.

Always use a new vial if you notice that your blood sugar control is unexpectedly getting worse. This is because the insulin may have lost some of its effectiveness. If you think you may have a problem with Toujeo, have it checked by your doctor or pharmacist.

**Insulin mix-ups**

You must always check the insulin label before each injection to avoid mix-ups between Toujeo and other insulins.

**If you use more Toujeo than you should**

- If you have injected too much Toujeo, your blood sugar level may become too low (hypoglycaemia).
Check your blood sugar frequently. In general, to prevent hypoglycaemia you must eat more food and monitor your blood sugar. For information on the treatment of hypoglycaemia, see box at the end of this leaflet.

If you forget to use Toujeo

- If you have missed a dose of Toujeo or if you have not injected enough insulin, your blood sugar level may become too high (hyperglycaemia). Check your blood sugar frequently. For information on the treatment of hyperglycaemia, see box at the end of this leaflet.
- Do not take a double dose to make up for a forgotten dose.

If you stop using Toujeo

This could lead to severe hyperglycaemia (very high blood sugar) and ketoacidosis (build-up of acid in the blood because the body is breaking down fat instead of sugar). Do not stop Toujeo without speaking to a doctor, who will tell you what needs to be done.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

If you notice signs of your blood sugar being too low (hypoglycaemia), take action to increase your blood sugar level straight away (see the box at the end of this leaflet). Hypoglycaemia (low blood sugar) can be very serious and is very common with insulin treatment (may affect more than 1 in 10 people). Low blood sugar means that there is not enough sugar in your blood. If your blood sugar level falls too low, you may pass out (become unconscious). Serious hypoglycaemia may cause brain damage and may be life-threatening. For more information, see the box at the end of this leaflet.

Severe allergic reactions (rare, may affect up to 1 in 1,000 people) – the signs may include large-scale skin reactions (rash and itching all over the body), severe swelling of skin or mucous membranes (angiooedema), shortness of breath, a fall in blood pressure with rapid heart beat and sweating. Severe allergic reactions to insulins may become life-threatening. Tell a doctor straight away if you notice signs of severe allergic reactions.

Common reported side effects (may affect up to 1 in 10 people)

• Skin changes at the injection site
If you inject your insulin too often at the same skin site, fatty tissue under the skin at this site may either shrink (lipoatrophy, may affect up to 1 in 100 people) or thicken (lipohypertrophy). The insulin may not work very well. Change the injection site with each injection to help prevent these skin changes.

• Skin and allergic reactions at the injection site
The signs may include reddening, unusually intense pain when injecting, itching, hives, swelling or inflammation. This can spread around the injection site. Most minor reactions to insulins usually disappear in a few days to a few weeks.

Rare reported side effect (may affect up to 1 in 1,000 people)

• Eye reactions
A marked change (improvement or worsening) in your blood sugar control can disturb your vision temporarily. If you have proliferative retinopathy (an eye disease related to diabetes) severe hypoglycaemic attacks may cause temporary loss of vision.

• General disorders
In rare cases, insulin treatment may also cause temporary build-up of water in the body, with swelling in the calves and ankles.
Very rare reported side-effects (may affect up to 1 in 10,000 people)
In very rare cases, dysgeusia (taste disorders) and myalgia (muscular pain) can occur.

Use in children and adolescents

In general, the side effects in children and adolescents of 18 years of age or less are similar to those seen in adults. Complaints of injection site reactions (injection site pain, injection site reaction) and skin reactions (rash, urticaria) are reported relatively more frequently in children and adolescents of 18 years of age or less than in adults. There is no experience in children under 2 years.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Toujeo

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and on the label of the vial after “EXP”. The expiry date refers to the last day of that month.

Unopened vials
Store in a refrigerator (2°C-8°C). Do not freeze or place next to the freezer or a freezer pack. Keep the vial in the outer carton in order to protect from light.

Opened vials
Once in use, the 5 ml vial may be stored for a maximum of 4 weeks in the outer carton not above 25°C and away from direct heat or direct light.
Once in use, the 10 ml vial may be stored for a maximum of 4 weeks in the outer carton not above 30°C and away from direct heat or direct light.
Do not use it after this time period. It is recommended that the date of the first use be noted on the label.

Do not use Toujeo if you notice particles in it. Only use Toujeo if the solution is clear, colourless and waterlike.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Toujeo contains

- The active substance is insulin glargine. Each ml of the solution contains 100 units of insulin glargine (equivalent to 3.64 mg).
- The other ingredients are: zinc chloride, metacresol, glycerol, sodium hydroxide (for pH adjustment) (see section 2 “Important information about some of the ingredients of Toujeo”), hydrochloric acid (for pH adjustment), polysorbate 20 (10 ml vial only) and water for injections.
What Toujeo looks like and contents of the pack

Toujeo 100 units/ml solution for injection in a vial is a clear colourless and waterlike solution. Each vial contains 5 ml of solution for injection (equivalent to 500 units) or 10 ml of solution for injection (equivalent to 1000 units). Pack sizes of 1, 2, 5 and 10 vials of 5 ml or 1 vial of 10 ml. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

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Other source of information
Detailed information on this medicine is available on the European Medicines Agency web site:
http://www.ema.europa.eu/
HYPERGLYCAEMIA AND HYPOGLYCAEMIA

Always carry some sugar (at least 20 grams) with you. Carry some information with you to show you are diabetic.

HYPERGLYCAEMIA (high blood sugar levels)

If your blood sugar is too high (hyperglycaemia), you may not have injected enough insulin.

Why does hyperglycaemia occur?
Examples include:
- you have not injected your insulin or not injected enough, or if it has become less effective, for example through incorrect storage,
- you are doing less exercise than usual, you are under stress (emotional distress, excitement), or you have an injury, operation, infection or fever,
- you are taking or have taken certain other medicines (see section 2, "Other medicines and Toujeo").

Warning symptoms of hyperglycaemia
Thirst, increased need to urinate, tiredness, dry skin, reddening of the face, loss of appetite, low blood pressure, fast heart beat and, glucose and ketone bodies in urine. Stomach pain, fast and deep breathing, sleepiness or even loss of consciousness may be signs of a serious condition (ketoacidosis) resulting from lack of insulin.

What should you do if you experience hyperglycaemia?
Test your blood sugar level and your urine for ketones as soon as any of the above symptoms occur. Severe hyperglycaemia or ketoacidosis must always be treated by a doctor, normally in a hospital.

HYPOGLYCAEMIA (low blood sugar levels)

If your blood sugar level falls too much you may become unconscious. Serious hypoglycaemia may cause a heart attack or brain damage and may be life-threatening. You normally should be able to recognise when your blood sugar is falling too much so that you can take the right actions.

Why does hypoglycaemia occur?
Examples include:
- you inject too much insulin,
- you miss meals or delay them,
- you do not eat enough, or eat food containing less carbohydrate than normal (sugar and substances similar to sugar are called carbohydrates; however, artificial sweeteners are NOT carbohydrates),
- you lose carbohydrates due to vomiting or diarrhoea,
- you drink alcohol, particularly if you are not eating much,
- you are doing more exercise than usual or a different type of physical activity,
- you are recovering from an injury or operation or other stress,
- you are recovering from an illness or from fever,
- you are taking or have stopped taking certain other medicines (see section 2, "Other medicines and Toujeo").
Hypoglycaemia is also more likely to occur if

- you have just begun insulin treatment or changed to another insulin preparation (when changing from your previous basal insulin to Toujeo hypoglycaemia, if it occurs, may be more likely to occur in the morning than at night),
- your blood sugar levels are almost normal or are unstable,
- you change the area of skin where you inject insulin (for example from the thigh to the upper arm),
- you suffer from severe kidney or liver disease, or some other disease such as hypothyroidism.

Warning symptoms of hypoglycaemia

- In your body
Examples of symptoms that tell you that your blood sugar level is falling too much or too fast: sweating, clammy skin, anxiety, fast heart beat, high blood pressure, palpitations and irregular heartbeat. These symptoms often develop before the symptoms of a low sugar level in the brain.

- In your brain
Examples of symptoms that indicate a low sugar level in the brain: headaches, intense hunger, nausea, vomiting, tiredness, sleepiness, sleep disturbances, restlessness, aggressive behaviour, lapses in concentration, impaired reactions, depression, confusion, speech disturbances (sometimes total loss of speech), visual disorders, trembling, paralysis, tingling sensations (paraesthesia), numbness and tingling sensations in the area of the mouth, dizziness, loss of self-control, inability to look after yourself, convulsions, loss of consciousness.

The first symptoms which alert you to hypoglycaemia ("warning symptoms") may change, be weaker or may be missing altogether if

- you are elderly, if you have had diabetes for a long time or if you suffer from a certain type of nervous disease (diabetic autonomic neuropathy),
- you have recently suffered hypoglycaemia (for example the day before) or if it develops slowly,
- you have almost normal or, at least, greatly improved blood sugar levels,
- you have recently changed from an animal insulin to a human insulin such as Toujeo,
- you are taking or have taken certain other medicines (see section 2, "Other medicines and Toujeo").

In such a case, you may develop severe hypoglycaemia (and even faint) before you are aware of the problem. Be familiar with your warning symptoms. If necessary, more frequent blood sugar testing can help to identify mild hypoglycaemic episodes that may otherwise be overlooked. If you are not confident about recognising your warning symptoms, avoid situations (such as driving a car) in which you or others would be put at risk by hypoglycaemia.

What should you do if you experience hypoglycaemia?

1. Do not inject insulin. Immediately take about 10 to 20 g sugar, such as glucose, sugar cubes or a sugar-sweetened beverage. Caution: Artificial sweeteners and foods with artificial sweeteners (such as diet drinks) are of no help in treating hypoglycaemia.
2. Then eat something that has a long-acting effect in raising your blood sugar (such as bread or pasta). Your doctor or nurse should have discussed this with you previously.
   The recovery of hypoglycaemia may be delayed because Toujeo has a long action.
3. If the hypoglycaemia comes back again take another 10 to 20 g sugar.
4. Speak to a doctor immediately if you are not able to control the hypoglycaemia or if it recurs.
Tell your relatives, friends and close colleagues the following:
If you are not able to swallow or if you are unconscious, you will require an injection of glucose or glucagon (a medicine which increases blood sugar). These injections are justified even if it is not certain that you have hypoglycaemia.

It is advisable to test your blood sugar immediately after taking glucose to check that you really have hypoglycaemia.
Read all of this leaflet carefully before you start using this medicine because it contains important information for you. The instructions for using the insulin pen are provided with your insulin pen. Refer to them before using your medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet
1. What Toujeo is and what it is used for
2. What you need to know before you use Toujeo
3. How to use Toujeo
4. Possible side effects
5. How to store Toujeo
6. Contents of the pack and other information

1. What Toujeo is and what it is used for

Toujeo contains insulin glargine. This is a modified insulin, very similar to human insulin.

Toujeo is used to treat diabetes mellitus in adults, adolescents and children aged 2 years and above. Diabetes mellitus is a disease where your body does not produce enough insulin to control the level of blood sugar. Insulin glargine has a long and steady blood-sugar-lowering action.

2. What you need to know before you use Toujeo

Do not use Toujeo

- If you are allergic to insulin glargine or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Toujeo. Follow closely the instructions for posology, monitoring (blood and urine tests), diet and physical activity (physical work and exercise) as discussed with your doctor.

If your blood sugar is too low (hypoglycaemia), follow the guidance for hypoglycaemia (see box at the end of this leaflet).

Travel

Before travelling consult your doctor. You may need to talk about
- the availability of your insulin in the country you are visiting,
- supplies of insulin, syringes etc.,
- correct storage of your insulin while travelling,
- timing of meals and insulin administration while travelling,
- the possible effects of changing to different time zones,
- possible new health risks in the countries to be visited,
- what you should do in emergency situations when you feel unwell or become ill.

**Illnesses and injuries**

In the following situations, the management of your diabetes may require a lot of care (for example, adjustment to insulin dose, blood and urine tests):
- If you are ill or have a major injury then your blood sugar level may increase (hyperglycaemia).
- If you are not eating enough your blood sugar level may become too low (hypoglycaemia).

In most cases you will need a doctor. **Make sure that you contact a doctor early.**

If you have type 1 diabetes (insulin dependent diabetes mellitus), do not stop your insulin and continue to get enough carbohydrates. Always tell people who are caring for you or treating you that you require insulin.

Insulin treatment can cause the body to produce antibodies to insulin (substances that act against insulin). However, only very rarely, this will require a change to your insulin dose.

Some patients with long-standing type 2 diabetes mellitus and heart disease or previous stroke who were treated with pioglitazone (oral anti-diabetic medicine used to treat type 2 diabetes mellitus) and insulin experienced the development of heart failure. Inform your doctor as soon as possible if you experience signs of heart failure such as unusual shortness of breath or rapid increase in weight or localised swelling (oedema).

**Children**

There is no experience with the use of Toujeo in children below the age of 2 years.

**Other medicines and Toujeo**

Some medicines cause changes in the blood sugar level (decrease, increase or both depending on the situation). In each case, it may be necessary to adjust your insulin dose to avoid blood sugar levels that are either too low or too high. Be careful when you start or stop taking another medicine.

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. Before taking a medicine ask your doctor if it can affect your blood sugar level and what action, if any, you need to take.

**Medicines that may cause your blood sugar level to fall (hypoglycaemia) include:**
- all other medicines to treat diabetes,
- angiotensin converting enzyme (ACE) inhibitors (used to treat certain heart conditions or high blood pressure),
- disopyramide (used to treat certain heart conditions),
- fluoxetine (used to treat depression),
- fibrates (used to lower high levels of blood lipids),
- monoamine oxidase (MAO) inhibitors (used to treat depression),
- pentoxifylline, propoxyphene, salicylates (such as acetylsalicylic acid, used to relieve pain and lower fever)
- sulphonamide antibiotics.

**Medicines that may cause your blood sugar level to rise (hyperglycaemia) include:**
- corticosteroids (such as "cortisone" used to treat inflammation),
- danazol (medicine acting on ovulation),
- diazoxide (used to treat high blood pressure),
- diuretics (used to treat high blood pressure or excessive fluid retention),
- glucagon (pancreas hormone used to treat severe hypoglycaemia),
- isoniazid (used to treat tuberculosis),
- oestrogens and progestogens (such as in the contraceptive pill used for birth control),
- phenothiazine derivatives (used to treat psychiatric disorders),
- somatropin (growth hormone),
- sympathomimetic medicines (such as epinephrine [adrenaline], salbutamol, terbutaline used to treat asthma),
- thyroid hormones (used to treat thyroid gland disorders),
- atypical antipsychotic medicines (such as clozapine, olanzapine),
- protease inhibitors (used to treat HIV).

**Your blood sugar level may either rise or fall if you take:**
- beta-blockers, (used to treat high blood pressure),
- clonidine (used to treat high blood pressure),
- lithium salts (used to treat psychiatric disorders).

Pentamidine (used to treat some infections caused by parasites) may cause hypoglycaemia which may sometimes be followed by hyperglycaemia.

Beta-blockers like other sympatholytic medicines (such as clonidine, guanethidine, and reserpine) may weaken or suppress entirely the first warning symptoms which help you to recognise a hypoglycaemia.

If you are not sure whether you are taking one of those medicines ask your doctor or pharmacist.

**Toujeo with alcohol**

Your blood sugar levels may either rise or fall if you drink alcohol.

**Pregnancy and breast-feeding**

Ask your doctor or pharmacist for advice before taking any medicine.

Inform your doctor if you are planning to become pregnant, or if you are already pregnant. Your insulin dose may need to be changed during pregnancy and after giving birth. Particularly careful control of your diabetes, and prevention of hypoglycaemia, is important for the health of your baby.

If you are breast-feeding consult your doctor as you may require adjustments in your insulin doses and your diet.

**Driving and using machines**

Your ability to concentrate or react may be reduced if:
- you have hypoglycaemia (low blood sugar levels),
- you have hyperglycaemia (high blood sugar levels),
- you have problems with your sight.

Keep this possible problem in mind in all situations where you might put yourself and others at risk (such as driving a car or using machines). You should contact your doctor for advice on driving if:
- you have frequent episodes of hypoglycaemia,
- the first warning symptoms which help you to recognise hypoglycaemia are reduced or absent.

**Important information about some of the ingredients of Toujeo**

This medicine contains less than 1 mmol (23 mg) sodium per dose, i.e. it is essentially ‘sodium-free’.  


3. **How to use Toujeo**

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

**Dose**

Based on your life-style and the results of your blood sugar (glucose) tests and your previous insulin usage, your doctor will:
- determine how much Toujeo per day you will need and at what time,
- tell you when to check your blood sugar level, and whether you need to carry out urine tests,
- tell you when you may need to inject a higher or lower dose of Toujeo.

Toujeo is a long-acting insulin. Your doctor may tell you to use it in combination with a short-acting insulin or with tablets used to treat high blood sugar levels.

Many factors may influence your blood sugar level. You should know these factors so that you are able to react correctly to changes in your blood sugar level and to prevent it from becoming too high or too low. See the box at the end of this leaflet for further information.

**Use in children and adolescents**

Toujeo can be used in adolescents and children aged 2 years and above. Use this medicine exactly as your doctor has told you.

**Frequency of administration**

You need one injection of Toujeo every day, at the same time of the day.

**Method of administration**

Toujeo is injected under the skin. Do NOT inject Toujeo in a vein, since this will change its action and may cause hypoglycaemia.

Your doctor will show you in which area of the skin you should inject Toujeo. With each injection, change the puncture site within the particular area of skin that you are using.

**How to handle the cartridges**

To ensure you get the accurate dose, the Toujeo cartridges are to be used only with the following pens:
- JuniorSTAR which delivers doses in steps of 0.5 units
- OptiPen, ClikSTAR, Tactipen, Autopen 24 or AllStar which deliver doses in steps of 1 unit.

Not all of these pens may be marketed in your country.

The pen should be used as recommended in the information provided by the device manufacturer. The manufacturer’s instructions for using the pen must be followed carefully for loading the cartridge, attaching the needle, and administering the insulin injection.

Keep the cartridge at room temperature for 1 or 2 hours before inserting it in the pen.

Look at the cartridge before you use it. Only use it if the solution is clear, colourless and waterlike, and has no visible particles in it.

Do not shake or mix it before use.

Always use a new cartridge if you notice that your blood sugar control is unexpectedly getting worse. This is because the insulin may have lost some of its effectiveness. If you think you may have a problem with Toujeo, have it checked by your doctor or pharmacist.
Special care before injection

Before injection remove any air bubbles (see instructions for using the pen).

Make sure that neither alcohol nor other disinfectants or other substances contaminate the insulin. Do not re-fill and re-use empty cartridges. Do not add any other insulin to the cartridge. Do not mix Toujeo with any other insulins or medicines. Do not dilute it. Mixing or diluting may change the action of Toujeo.

Problems with the insulin pen?

Refer to the manufacturer’s instructions for using the pen.
If the insulin pen is damaged or not working properly (due to mechanical defects) it has to be discarded, and a new insulin pen has to be used.

If the insulin pen does not function well, you can draw the insulin from the cartridge into a syringe for injection. Therefore, keep injection syringes and needles as well. However, use only injection syringes which are designed for an insulin concentration of 100 units per millilitre.

Insulin mix-ups

You must always check the insulin label before each injection to avoid mix-ups between Toujeo and other insulins.

If you use more Toujeo than you should

- If you have injected too much Toujeo, your blood sugar level may become too low (hypoglycaemia).
  Check your blood sugar frequently. In general, to prevent hypoglycaemia you must eat more food and monitor your blood sugar. For information on the treatment of hypoglycaemia, see box at the end of this leaflet.

If you forget to use Toujeo

- If you have missed a dose of Toujeo or if you have not injected enough insulin, your blood sugar level may become too high (hyperglycaemia). Check your blood sugar frequently.
  For information on the treatment of hyperglycaemia, see box at the end of this leaflet.
- Do not take a double dose to make up for a forgotten dose.

If you stop using Toujeo

This could lead to severe hyperglycaemia (very high blood sugar) and ketoacidosis (build-up of acid in the blood because the body is breaking down fat instead of sugar). Do not stop Toujeo without speaking to a doctor, who will tell you what needs to be done.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

If you notice signs of your blood sugar being too low (hypoglycaemia), take action to increase your blood sugar level straight away (see the box at the end of this leaflet). Hypoglycaemia (low blood sugar) can be very serious and is very common with insulin treatment (may affect more than 1 in 10 people). Low blood sugar means that there is not enough sugar in your blood. If your blood sugar level
falls too low, you may pass out (become unconscious). Serious hypoglycaemia may cause brain damage and may be life-threatening. For more information, see the box at the end of this leaflet.

Severe allergic reactions (rare, may affect up to 1 in 1,000 people) – the signs may include large-scale skin reactions (rash and itching all over the body), severe swelling of skin or mucous membranes (angiooedema), shortness of breath, a fall in blood pressure with rapid heart beat and sweating. Severe allergic reactions to insulins may become life-threatening. Tell a doctor straight away if you notice signs of severe allergic reactions.

Common reported side effects (may affect up to 1 in 10 people)

• Skin changes at the injection site
  If you inject your insulin too often at the same skin site, fatty tissue under the skin at this site may either shrink (lipoatrophy, may affect up to 1 in 100 people) or thicken (lipohypertrophy). The insulin may not work very well. Change the injection site with each injection to help prevent these skin changes.

• Skin and allergic reactions at the injection site
  The signs may include reddening, unusually intense pain when injecting, itching, hives, swelling or inflammation. This can spread around the injection site. Most minor reactions to insulins usually disappear in a few days to a few weeks.

Rare reported side effect (may affect up to 1 in 1,000 people)

• Eye reactions
  A marked change (improvement or worsening) in your blood sugar control can disturb your vision temporarily. If you have proliferative retinopathy (an eye disease related to diabetes) severe hypoglycaemic attacks may cause temporary loss of vision.

• General disorders
  In rare cases, insulin treatment may also cause temporary build-up of water in the body, with swelling in the calves and ankles.

Very rare reported side-effects (may affect up to 1 in 10,000 people)

In very rare cases, dysgeusia (taste disorders) and myalgia (muscular pain) can occur.

Use in children and adolescents

In general, the side effects in children and adolescents of 18 years of age or less are similar to those seen in adults.
Complaints of injection site reactions (injection site pain, injection site reaction) and skin reactions (rash, urticaria) are reported relatively more frequently in children and adolescents of 18 years of age or less than in adults.
There is no experience in children under 2 years.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Toujeo

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and on the label of the cartridge after “EXP”. The expiry date refers to the last day of that month.
Unopened cartridges
Store in a refrigerator (2°C-8°C). Do not freeze or place next to the freezer or a freezer pack. Keep the cartridge in the outer carton in order to protect from light.

In use cartridges
Cartridges in use (in the insulin pen) or carried as a spare may be stored for a maximum of 4 weeks not above 30°C and away from direct heat or direct light. The cartridge in use in the insulin pen must not be stored in a refrigerator.
Do not use it after this time period.

Do not use Toujeo if you notice particles in it. Only use Toujeo if the solution is clear, colourless and waterlike.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Toujeo contains
- The active substance is insulin glargine. Each ml of the solution contains 100 units of insulin glargine (equivalent to 3.64 mg).
- The other ingredients are: zinc chloride, metacresol, glycerol, sodium hydroxide (for pH adjustment) (see section 2 “Important information about some of the ingredients of Toujeo”), hydrochloric acid (for pH adjustment) and water for injections.

What Toujeo looks like and contents of the pack
Toujeo 100 units/ml solution for injection in a cartridge is a clear and colourless solution.

Toujeo comes in a special cartridge to be used only in conjunction with the pens OptiPen, ClikSTAR, Tactipen, Autopen 24, AllStar or JuniorSTAR. Each cartridge contains 3 ml of solution for injection (equivalent to 300 units).
Packs of 4, 5 and 10 cartridges.
Not all pack sizes may be marketed.

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For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder.

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Other source of information  
Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu/
HYPERGLYCAEMIA AND HYPOGLYCAEMIA

Always carry some sugar (at least 20 grams) with you. Carry some information with you to show you are diabetic.

HYPERGLYCAEMIA (high blood sugar levels)

If your blood sugar is too high (hyperglycaemia), you may not have injected enough insulin.

Why does hyperglycaemia occur?
Examples include:
- you have not injected your insulin or not injected enough, or if it has become less effective, for example through incorrect storage,
- your insulin pen does not work properly,
- you are doing less exercise than usual, you are under stress (emotional distress, excitement), or you have an injury, operation, infection or fever,
- you are taking or have taken certain other medicines (see section 2, "Other medicines and Toujeo").

Warning symptoms of hyperglycaemia
Thirst, increased need to urinate, tiredness, dry skin, reddening of the face, loss of appetite, low blood pressure, fast heart beat, and, glucose and ketone bodies in urine. Stomach pain, fast and deep breathing, sleepiness or even loss of consciousness may be signs of a serious condition (ketoacidosis) resulting from lack of insulin.

What should you do if you experience hyperglycaemia?
Test your blood sugar level and your urine for ketones as soon as any of the above symptoms occur. Severe hyperglycaemia or ketoacidosis must always be treated by a doctor, normally in a hospital.

HYPOGLYCAEMIA (low blood sugar levels)

If your blood sugar level falls too much you may become unconscious. Serious hypoglycaemia may cause a heart attack or brain damage and may be life-threatening. You normally should be able to recognise when your blood sugar is falling too much so that you can take the right actions.

Why does hypoglycaemia occur?
Examples include:
- you inject too much insulin,
- you miss meals or delay them,
- you do not eat enough, or eat food containing less carbohydrate than normal (sugar and substances similar to sugar are called carbohydrates; however, artificial sweeteners are NOT carbohydrates),
- you lose carbohydrates due to vomiting or diarrhoea,
- you drink alcohol, particularly if you are not eating much,
- you are doing more exercise than usual or a different type of physical activity,
- you are recovering from an injury or operation or other stress,
- you are recovering from an illness or from fever,
- you are taking or have stopped taking certain other medicines (see section 2, "Other medicines and Toujeo").
Hypoglycaemia is also more likely to occur if
- you have just begun insulin treatment or changed to another insulin preparation (when changing from your previous basal insulin to Toujeo hypoglycaemia, if it occurs, may be more likely to occur in the morning than at night),
- your blood sugar levels are almost normal or are unstable,
- you change the area of skin where you inject insulin (for example from the thigh to the upper arm),
- you suffer from severe kidney or liver disease, or some other disease such as hypothyroidism.

Warning symptoms of hypoglycaemia

-In your body
Examples of symptoms that tell you that your blood sugar level is falling too much or too fast: sweating, clammy skin, anxiety, fast heart beat, high blood pressure, palpitations and irregular heartbeat. These symptoms often develop before the symptoms of a low sugar level in the brain.

-In your brain
Examples of symptoms that indicate a low sugar level in the brain: headaches, intense hunger, nausea, vomiting, tiredness, sleepiness, sleep disturbances, restlessness, aggressive behaviour, lapses in concentration, impaired reactions, depression, confusion, speech disturbances (sometimes total loss of speech), visual disorders, trembling, paralysis, tingling sensations (paraesthesia), numbness and tingling sensations in the area of the mouth, dizziness, loss of self-control, inability to look after yourself, convulsions, loss of consciousness.

The first symptoms which alert you to hypoglycaemia ("warning symptoms") may change, be weaker or may be missing altogether if
- you are elderly, if you have had diabetes for a long time or if you suffer from a certain type of nervous disease (diabetic autonomic neuropathy),
- you have recently suffered hypoglycaemia (for example the day before) or if it develops slowly,
- you have almost normal or, at least, greatly improved blood sugar levels,
- you have recently changed from an animal insulin to a human insulin such as Toujeo,
- you are taking or have taken certain other medicines (see section 2, "Other medicines and Toujeo").

In such a case, you may develop severe hypoglycaemia (and even faint) before you are aware of the problem. Be familiar with your warning symptoms. If necessary, more frequent blood sugar testing can help to identify mild hypoglycaemic episodes that may otherwise be overlooked. If you are not confident about recognising your warning symptoms, avoid situations (such as driving a car) in which you or others would be put at risk by hypoglycaemia.

What should you do if you experience hypoglycaemia?

1. Do not inject insulin. Immediately take about 10 to 20 g sugar, such as glucose, sugar cubes or a sugar-sweetened beverage. Caution: Artificial sweeteners and foods with artificial sweeteners (such as diet drinks) are of no help in treating hypoglycaemia.
2. Then eat something that has a long-acting effect in raising your blood sugar (such as bread or pasta). Your doctor or nurse should have discussed this with you previously.
   The recovery of hypoglycaemia may be delayed because Toujeo has a long action.
3. If the hypoglycaemia comes back again take another 10 to 20 g sugar.
4. Speak to a doctor immediately if you are not able to control the hypoglycaemia or if it recurs.
Tell your relatives, friends and close colleagues the following:
If you are not able to swallow or if you are unconscious, you will require an injection of glucose or glucagon (a medicine which increases blood sugar). These injections are justified even if it is not certain that you have hypoglycaemia.

It is advisable to test your blood sugar immediately after taking glucose to check that you really have hypoglycaemia.
Package leaflet: Information for the user

Toujeo 100 units/ml solution for injection in a cartridge for OptiClik
Insulin glargine

Read all of this leaflet carefully before you start using this medicine because it contains important information for you. The instructions for using OptiClik, the insulin pen, are provided with your OptiClik. Refer to them before using your medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet
1. What Toujeo is and what it is used for
2. What you need to know before you use Toujeo
3. How to use Toujeo
4. Possible side effects
5. How to store Toujeo
6. Contents of the pack and other information

1. What Toujeo is and what it is used for

Toujeo contains insulin glargine. This is a modified insulin, very similar to human insulin.

Toujeo is used to treat diabetes mellitus in adults, adolescents and children aged 2 years and above. Diabetes mellitus is a disease where your body does not produce enough insulin to control the level of blood sugar. Insulin glargine has a long and steady blood-sugar-lowering action.

2. What you need to know before you use Toujeo

Do not use Toujeo

- If you are allergic to insulin glargine or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Toujeo. Follow closely the instructions for posology, monitoring (blood and urine tests), diet and physical activity (physical work and exercise) as discussed with your doctor.

If your blood sugar is too low (hypoglycaemia), follow the guidance for hypoglycaemia (see box at the end of this leaflet).
Travel

Before travelling consult your doctor. You may need to talk about
- the availability of your insulin in the country you are visiting,
- supplies of insulin, syringes etc.,
- correct storage of your insulin while travelling,
- timing of meals and insulin administration while travelling,
- the possible effects of changing to different time zones,
- possible new health risks in the countries to be visited,
- what you should do in emergency situations when you feel unwell or become ill.

Illnesses and injuries

In the following situations, the management of your diabetes may require a lot of care (for example, adjustment to insulin dose, blood and urine tests):
- If you are ill or have a major injury then your blood sugar level may increase (hyperglycaemia).
- If you are not eating enough your blood sugar level may become too low (hypoglycaemia).

In most cases you will need a doctor. Make sure that you contact a doctor early.

If you have type 1 diabetes (insulin dependent diabetes mellitus), do not stop your insulin and continue to get enough carbohydrates. Always tell people who are caring for you or treating you that you require insulin.

Insulin treatment can cause the body to produce antibodies to insulin (substances that act against insulin). However, only very rarely, this will require a change to your insulin dose.

Some patients with long-standing type 2 diabetes mellitus and heart disease or previous stroke who were treated with pioglitazone (oral anti-diabetic medicine used to treat type 2 diabetes mellitus) and insulin experienced the development of heart failure. Inform your doctor as soon as possible if you experience signs of heart failure such as unusual shortness of breath or rapid increase in weight or localised swelling (oedema).

Children

There is no experience with the use of Toujeo in children below the age of 2 years.

Other medicines and Toujeo

Some medicines cause changes in the blood sugar level (decrease, increase or both depending on the situation). In each case, it may be necessary to adjust your insulin dose to avoid blood sugar levels that are either too low or too high. Be careful when you start or stop taking another medicine.

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. Before taking a medicine ask your doctor if it can affect your blood sugar level and what action, if any, you need to take.

Medicines that may cause your blood sugar level to fall (hypoglycaemia) include:
- all other medicines to treat diabetes,
- angiotensin converting enzyme (ACE) inhibitors (used to treat certain heart conditions or high blood pressure),
- disopyramide (used to treat certain heart conditions),
- fluoxetine (used to treat depression),
- fibrates (used to lower high levels of blood lipids),
- monoamine oxidase (MAO) inhibitors (used to treat depression),
- pentoxifylline, propoxyphene, salicylates (such as acetylsalicylic acid, used to relieve pain and lower fever),
- sulfonamide antibiotics.
Medicines that may cause your blood sugar level to rise (hyperglycaemia) include:
- corticosteroids (such as "cortisone", used to treat inflammation),
- danazol (medicine acting on ovulation),
- diazoxide (used to treat high blood pressure),
- diuretics (used to treat high blood pressure or excessive fluid retention),
- glucagon (pancreas hormone used to treat severe hypoglycaemia),
- isoniazid (used to treat tuberculosis),
- oestrogens and progestogens (such as in the contraceptive pill used for birth control),
- phenothiazine derivatives (used to treat psychiatric disorders),
- somatropin (growth hormone),
- sympathomimetic medicines (such as epinephrine [adrenaline], salbutamol, terbutaline used to treat asthma),
- thyroid hormones (used to treat thyroid gland disorders),
- atypical antipsychotic medicines (such as clozapine, olanzapine),
- protease inhibitors (used to treat HIV).

Your blood sugar level may either rise or fall if you take:
- beta-blockers (used to treat high blood pressure),
- clonidine (used to treat high blood pressure),
- lithium salts (used to treat psychiatric disorders).

Pentamidine (used to treat some infections caused by parasites) may cause hypoglycaemia which may sometimes be followed by hyperglycaemia.

Beta-blockers like other sympatholytic medicines (such as clonidine, guanethidine, and reserpine) may weaken or suppress entirely the first warning symptoms which help you to recognise a hypoglycaemia.

If you are not sure whether you are taking one of those medicines ask your doctor or pharmacist.

**Toujeo with alcohol**

Your blood sugar levels may either rise or fall if you drink alcohol.

**Pregnancy and breast-feeding**

Ask your doctor or pharmacist for advice before taking any medicine.

Inform your doctor if you are planning to become pregnant, or if you are already pregnant. Your insulin dose may need to be changed during pregnancy and after giving birth. Particularly careful control of your diabetes, and prevention of hypoglycaemia, is important for the health of your baby.

If you are breast-feeding consult your doctor as you may require adjustments in your insulin doses and your diet.

**Driving and using machines**

Your ability to concentrate or react may be reduced if:
- you have hypoglycaemia (low blood sugar levels),
- you have hyperglycaemia (high blood sugar levels),
- you have problems with your sight.

Keep this possible problem in mind in all situations where you might put yourself and others at risk (such as driving a car or using machines). You should contact your doctor for advice on driving if:
- you have frequent episodes of hypoglycaemia,
- the first warning symptoms which help you to recognise hypoglycaemia are reduced or absent.
3. **How to use Toujeo**

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

**Dose**

Based on your life-style and the results of your blood sugar (glucose) tests and your previous insulin usage, your doctor will
- determine how much Toujeo per day you will need and at what time,
- tell you when to check your blood sugar level, and whether you need to carry out urine tests,
- tell you when you may need to inject a higher or lower dose of Toujeo.

Toujeo is a long-acting insulin. Your doctor may tell you to use it in combination with a short-acting insulin or with tablets used to treat high blood sugar levels.

Many factors may influence your blood sugar level. You should know these factors so that you are able to react correctly to changes in your blood sugar level and to prevent it from becoming too high or too low. See the box at the end of this leaflet for further information.

**Use in children and adolescents**

Toujeo can be used in adolescents and children aged 2 years and above. Use this medicine exactly as your doctor has told you.

**Frequency of administration**

You need one injection of Toujeo every day, at the same time of the day.

**Method of administration**

Toujeo is injected under the skin. Do NOT inject Toujeo in a vein, since this will change its action and may cause hypoglycaemia.

Your doctor will show you in which area of the skin you should inject Toujeo. With each injection, change the puncture site within the particular area of skin that you are using.

**How to handle the cartridges for OptiClik**

Toujeo in cartridge for OptiClik has been developed for use in OptiClik only. The manufacturer’s instructions for using the pen must be followed carefully for loading the cartridge, attaching the needle, and administering the insulin injection.

Keep the cartridge at room temperature for 1 or 2 hours before inserting it in the pen. Look at the cartridge before you use it. Only use it if the solution is clear, colourless and waterlike, and has no visible particles in it. Do not shake or mix it before use.

Always use a new cartridge if you notice that your blood sugar control is unexpectedly getting worse. This is because the insulin may have lost some of its effectiveness. If you think you may have a problem with Toujeo, have it checked by your doctor or pharmacist.
Special care before injection

Before injection remove any air bubbles (see instructions for using the pen). Make sure that neither alcohol nor other disinfectants or other substances contaminate the insulin. Do not re-fill and re-use empty cartridges. Do not add any other insulin to the cartridge. Do not mix Toujeo with any other insulins or medicines. Do not dilute it. Mixing or diluting may change the action of Toujeo.

Problems with OptiClik?

Refer to the manufacturer’s instructions for using the pen. If OptiClik is damaged or not working properly (due to mechanical defects) it has to be discarded, and a new OptiClik has to be used.

If OptiClik does not function well, you can draw the insulin from the cartridge into a syringe for injection. Therefore, keep injection syringes and needles as well. However, use only injection syringes which are designed for an insulin concentration of 100 Units per millilitre.

Insulin Mix-ups

You must always check the insulin label before each injection to avoid mix-ups between Toujeo and other insulins.

If you use more Toujeo than you should

- If you have injected too much Toujeo, your blood sugar level may become too low (hypoglycaemia). Check your blood sugar frequently. In general, to prevent hypoglycaemia you must eat more food and monitor your blood sugar. For information on the treatment of hypoglycaemia, see box at the end of this leaflet.

If you forget to use Toujeo

- If you have missed a dose of Toujeo or if you have not injected enough insulin, your blood sugar level may become too high (hyperglycaemia). Check your blood sugar frequently. For information on the treatment of hyperglycaemia, see box at the end of this leaflet.
- Do not take a double dose to make up for a forgotten dose.

If you stop using Toujeo

This could lead to severe hyperglycaemia (very high blood sugar) and ketoacidosis (build-up of acid in the blood because the body is breaking down fat instead of sugar). Do not stop Toujeo without speaking to a doctor, who will tell you what needs to be done.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

If you notice signs of your blood sugar being too low (hypoglycaemia), take action to increase your blood sugar level straight away (see the box at the end of this leaflet). Hypoglycaemia (low blood sugar) can be very serious and is very common with insulin treatment (may affect more than 1 in 10 people). Low blood sugar means that there is not enough sugar in your blood. If your blood sugar level falls too low, you may pass out (become unconscious). Serious hypoglycaemia may cause brain damage and may be life-threatening. For more information, see the box at the end of this leaflet.
**Severe allergic reactions** (rare, may affect up to 1 in 1,000 people) – the signs may include large-scale skin reactions (rash and itching all over the body), severe swelling of skin or mucous membranes (angiooedema), shortness of breath, a fall in blood pressure with rapid heart beat and sweating. Severe allergic reactions to insulins may become life-threatening. Tell a doctor straight away if you notice signs of severe allergic reactions.

**Common reported side effects** (may affect up to 1 in 10 people)
- **Skin changes at the injection site**
  If you inject your insulin too often at the same skin site, fatty tissue under the skin at this site may either shrink (lipatrophy, may affect up to 1 in 100 people) or thicken (lipohypertrophy). The insulin may not work very well. Change the injection site with each injection to help to prevent these skin changes.

- **Skin and allergic reactions at the injection site**
  The signs may include reddening, unusually intense pain when injecting, itching, hives, swelling or inflammation. This can spread around the injection site. Most minor reactions to insulins usually disappear in a few days to a few weeks.

**Rare reported side effect** (may affect up to 1 in 1,000 people)
- **Eye reactions**
  A marked change (improvement or worsening) in your blood sugar control can disturb your vision temporarily. If you have proliferative retinopathy (an eye disease related to diabetes) severe hypoglycaemic attacks may cause temporary loss of vision.

- **General disorders**
  In rare cases, insulin treatment may also cause temporary build-up of water in the body, with swelling in the calves and ankles.

**Rare reported side-effects** (may affect up to 1 in 10,000 people)
- In very rare cases, dysgeusia (taste disorders) and myalgia (muscular pain) can occur.

**Use in children and adolescents**

In general, the side effects in children and adolescents of 18 years of age or less are similar to those seen in adults.

Complaints of injection site reactions (injection site pain, injection site reaction) and skin reactions (rash, urticaria) are reported relatively more frequently in children and adolescents of 18 years of age or less than in adults.

There is no experience in children under 2 years.

**Reporting of side effects**

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. **How to store Toujeo**

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and on the label of the cartridge after “EXP”. The expiry date refers to the last day of that month.

**Unopened cartridges**

Store in a refrigerator (2°C-8°C).

Do not freeze or place next to the freezer compartment or a freezer pack. Keep the cartridge in the outer carton in order to protect from light.
In-use cartridges
Cartridges in use (in the insulin pen) or carried as a spare may be stored for a maximum of 4 weeks not above 30°C and away from direct heat or direct light. The cartridge in use in the insulin pen must not be stored in the refrigerator. Do not use it after this time period.

Do not use Toujeo if you notice particles in it. Only use Toujeo if the solution is clear, colourless and waterlike.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Toujeo contains
- The active substance is insulin glargine. Each ml of the solution contains 100 units of insulin glargine (equivalent to 3.64 mg).
- The other ingredients are: zinc chloride, m-cresol, glycerol, sodium hydroxide (for pH adjustment) (see section 2 “Important information about some of the ingredients of Toujeo”), hydrochloric acid (for pH adjustment) and water for injections.

What Toujeo looks like and contents of the pack

Toujeo 100 units/ml solution for injection in a cartridge for OptiClik is a clear, colourless solution. This cartridge is for use with OptiClik only.

Toujeo comes in a cartridge sealed in a plastic container, which is the disposable part of OptiClik, an Insulin Pen. Each cartridge contains 3 ml of solution for injection (equivalent to 300 units).
Pack sizes of 1, 3, 4, 5, 6, 8, 9 and 10 cartridges.
Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

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For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder.

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Other source of information
Detailed information on this medicine is available on the European Medicines Agency web site:
http://www.ema.europa.eu/
HYPERGLYCAEMIA AND HYPOGLYCAEMIA

Always carry some sugar (at least 20 grams) with you. Carry some information with you to show you are diabetic.

HYPERGLYCAEMIA (high blood sugar levels)

If your blood sugar is too high (hyperglycaemia), you may not have injected enough insulin.

Why does hyperglycaemia occur?
Examples include:
- you have not injected your insulin or not injected enough, or if it has become less effective, for example through incorrect storage,
- your insulin pen does not work properly,
- you are doing less exercise than usual, you are under stress (emotional distress, excitement), or you have an injury, operation, infection or fever,
- you are taking or have taken certain other medicines (see section 2, "Other medicines and Toujeo").

Warning symptoms of hyperglycaemia
Thirst, increased need to urinate, tiredness, dry skin, reddening of the face, loss of appetite, low blood pressure, fast heart beat, and glucose and ketone bodies in urine. Stomach pain, fast and deep breathing, sleepiness or even loss of consciousness may be signs of a serious condition (ketoacidosis) resulting from lack of insulin.

What should you do if you experience hyperglycaemia?
Test your blood sugar level and your urine for ketones as soon as any of the above symptoms occur. Severe hyperglycaemia or ketoacidosis must always be treated by a doctor, normally in a hospital.

HYPOGLYCAEMIA (low blood sugar levels)

If your blood sugar level falls too much you may become unconscious. Serious hypoglycaemia may cause a heart attack or brain damage and may be life-threatening. You normally should be able to recognise when your blood sugar is falling too much so that you can take the right actions.

Why does hypoglycaemia occur?
Examples include:
- you inject too much insulin,
- you miss meals or delay them,
- you do not eat enough, or eat food containing less carbohydrate than normal (sugar and substances similar to sugar are called carbohydrates; however, artificial sweeteners are NOT carbohydrates),
- you lose carbohydrates due to vomiting or diarrhoea,
- you drink alcohol, particularly if you are not eating much,
- you are doing more exercise than usual or a different type of physical activity,
- you are recovering from an injury or operation or other stress,
- you are recovering from an illness or from fever,
- you are taking or have stopped taking certain other medicines (see section 2, "Other medicines and Toujeo").
Hypoglycaemia is also more likely to occur if:
- you have just begun insulin treatment or changed to another insulin preparation (when changing from your previous basal insulin to Toujeo hypoglycaemia, if it occurs, may be more likely to occur in the morning than at night),
- your blood sugar levels are almost normal or are unstable,
- you change the area of skin where you inject insulin (for example from the thigh to the upper arm),
- you suffer from severe kidney or liver disease, or some other disease such as hypothyroidism.

Warning symptoms of hypoglycaemia

- In your body
Examples of symptoms that tell you that your blood sugar level is falling too much or too fast: sweating, clammy skin, anxiety, fast heart beat, high blood pressure, palpitations and irregular heartbeat. These symptoms often develop before the symptoms of a low sugar level in the brain.

- In your brain
Examples of symptoms that indicate a low sugar level in the brain: headaches, intense hunger, nausea, vomiting, tiredness, sleepiness, sleep disturbances, restlessness, aggressive behaviour, lapses in concentration, impaired reactions, depression, confusion, speech disturbances (sometimes total loss of speech), visual disorders, trembling, paralysis, tingling sensations (paraesthesia), numbness and tingling sensations in the area of the mouth, dizziness, loss of self-control, inability to look after yourself, convulsions, loss of consciousness.

The first symptoms which alert you to hypoglycaemia ("warning symptoms") may change, be weaker or may be missing altogether if
- you are elderly, if you have had diabetes for a long time or if you suffer from a certain type of nervous disease (diabetic autonomic neuropathy),
- you have recently suffered hypoglycaemia (for example the day before) or if it develops slowly,
- you have almost normal or, at least, greatly improved blood sugar levels,
- you have recently changed from an animal insulin to a human insulin such as Toujeo,
- you are taking or have taken certain other medicines (see section 2, "Other medicines and Toujeo").

In such a case, you may develop severe hypoglycaemia (and even faint) before you are aware of the problem. Be familiar with your warning symptoms. If necessary, more frequent blood sugar testing can help to identify mild hypoglycaemic episodes that may otherwise be overlooked. If you are not confident about recognising your warning symptoms, avoid situations (such as driving a car) in which you or others would be put at risk by hypoglycaemia.

What should you do if you experience hypoglycaemia?

1. Do not inject insulin. Immediately take about 10 to 20 g sugar, such as glucose, sugar cubes or a sugar-sweetened beverage. Caution: Artificial sweeteners and foods with artificial sweeteners (such as diet drinks) are of no help in treating hypoglycaemia.
2. Then eat something that has a long-acting effect in raising your blood sugar (such as bread or pasta). Your doctor or nurse should have discussed this with you previously.
   The recovery of hypoglycaemia may be delayed because Toujeo has a long action.
3. If the hypoglycaemia comes back again take another 10 to 20 g sugar.
4. Speak to a doctor immediately if you are not able to control the hypoglycaemia or if it recurs.
Tell your relatives, friends and close colleagues the following:
If you are not able to swallow or if you are unconscious, you will require an injection of glucose or glucagon (a medicine which increases blood sugar). These injections are justified even if it is not certain that you have hypoglycaemia.

It is advisable to test your blood sugar immediately after taking glucose to check that you really have hypoglycaemia.
Read all of this leaflet carefully including the Instructions for Use of Toujeo OptiSet, pre-filled pen, before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet
1. What Toujeo is and what it is used for
2. What you need to know before you use Toujeo
3. How to use Toujeo
4. Possible side effects
5. How to store Toujeo
6. Contents of the pack and other information

1. What Toujeo is and what it is used for

Toujeo contains insulin glargine. This is a modified insulin, very similar to human insulin.

Toujeo is used to treat diabetes mellitus in adults, adolescents and children aged 2 years and above. Diabetes mellitus is a disease where your body does not produce enough insulin to control the level of blood sugar. Insulin glargine has a long and steady blood-sugar-lowering action.

2. What you need to know before you use Toujeo

Do not use Toujeo

- If you are allergic to insulin glargine or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Toujeo. Follow closely the instructions for posology, monitoring (blood and urine tests), diet and physical activity (physical work and exercise), injection technique as discussed with your doctor.

If your blood sugar is too low (hypoglycaemia), follow the guidance for hypoglycaemia (see box at the end of this leaflet).
Travel

Before travelling consult your doctor. You may need to talk about
- the availability of your insulin in the country you are visiting,
- supplies of insulin, syringes etc.,
- correct storage of your insulin while travelling,
- timing of meals and insulin administration while travelling,
- the possible effects of changing to different time zones,
- possible new health risks in the countries to be visited,
- what you should do in emergency situations when you feel unwell or become ill.

Illnesses and injuries

In the following situations, the management of your diabetes may require a lot of care (for example, adjustment to insulin dose, blood and urine tests):
- If you are ill or have a major injury then your blood sugar level may increase (hyperglycaemia).
- If you are not eating enough your blood sugar level may become too low (hypoglycaemia).

In most cases you will need a doctor. **Make sure that you contact a doctor early.**

If you have type 1 diabetes (insulin dependent diabetes mellitus), do not stop your insulin and continue to get enough carbohydrates. Always tell people who are caring for you or treating you that you require insulin.

Insulin treatment can cause the body to produce antibodies to insulin (substances that act against insulin). However, only very rarely, this will require a change to your insulin dose.

Some patients with long-standing type 2 diabetes mellitus and heart disease or previous stroke who were treated with pioglitazone (oral anti-diabetic medicine used to treat type 2 diabetes mellitus) and insulin experienced the development of heart failure. Inform your doctor as soon as possible if you experience signs of heart failure such as unusual shortness of breath or rapid increase in weight or localised swelling (oedema).

Children

There is no experience with the use of Toujeo in children below the age of 2 years.

Other medicines and Toujeo

Some medicines cause changes in the blood sugar level (decrease, increase or both depending on the situation). In each case, it may be necessary to adjust your insulin dose to avoid blood sugar levels that are either too low or too high. Be careful when you start or stop taking another medicine.

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. Before taking a medicine ask your doctor if it can affect your blood sugar level and what action, if any, you need to take.

**Medicines that may cause your blood sugar level to fall (hypoglycaemia) include:**
- all other medicines to treat diabetes,
- angiotensin converting enzyme (ACE) inhibitors (used to treat certain heart conditions or high blood pressure),
- disopyramide (used to treat certain heart conditions),
- fluoxetine (used to treat depression),
- fibrates (used to lower high levels of blood lipids),
- monoamine oxidase (MAO) inhibitors (used to treat depression),
- pentoxyfylline, propoxyphene, salicylates (such as acetylsalicylic acid, used to relieve pain and lower fever),
- sulfonamide antibiotics.
Medicines that may cause your blood sugar level to rise (hyperglycaemia) include:

- corticosteroids (such as "cortisone" used to treat inflammation),
- danazol (medicine acting on ovulation),
- diazoxide (used to treat high blood pressure),
- diuretics (used to treat high blood pressure or excessive fluid retention),
- glucagon (pancreas hormone used to treat severe hypoglycaemia),
- isoniazid (used to treat tuberculosis),
- oestrogens and progestogens (such as in the contraceptive pill used for birth control),
- phenothiazine derivatives (used to treat psychiatric disorders),
- somatropin (growth hormone),
- sympathomimetic medicines (such as epinephrine [adrenaline], salbutamol, terbutaline used to treat asthma),
- thyroid hormones (used to treat thyroid gland disorders),
- atypical antipsychotic medicines (such as clozapine, olanzapine),
- protease inhibitors (used to treat HIV).

Your blood sugar level may either rise or fall if you take:

- beta-blockers (used to treat high blood pressure),
- clonidine (used to treat high blood pressure),
- lithium salts (used to treat psychiatric disorders).

Pentamidine (used to treat some infections caused by parasites) may cause hypoglycaemia which may sometimes be followed by hyperglycaemia.

Beta-blockers like other sympatholytic medicines (such as clonidine, guanethidine, and reserpine) may weaken or suppress entirely the first warning symptoms which help you to recognise a hypoglycaemia.

If you are not sure whether you are taking one of those medicines ask your doctor or pharmacist.

**Toujeo with alcohol**

Your blood sugar levels may either rise or fall if you drink alcohol.

**Pregnancy and breast-feeding**

Ask your doctor or pharmacist for advice before taking any medicine.

Inform your doctor if you are planning to become pregnant, or if you are already pregnant. Your insulin dose may need to be changed during pregnancy and after giving birth. Particularly careful control of your diabetes, and prevention of hypoglycaemia, is important for the health of your baby.

If you are breast-feeding consult your doctor as you may require adjustments in your insulin doses and your diet.

**Driving and using machines**

Your ability to concentrate or react may be reduced if:

- you have hypoglycaemia (low blood sugar levels),
- you have hyperglycaemia (high blood sugar levels),
- you have problems with your sight.

Keep this possible problem in mind in all situations where you might put yourself and others at risk (such as driving a car or using machines). You should contact your doctor for advice on driving if:

- you have frequent episodes of hypoglycaemia,
- the first warning symptoms which help you to recognise hypoglycaemia are reduced or absent.
Important information about some of the ingredients of Toujeo

This medicine contains less than 1 mmol (23 mg) sodium per dose, i.e. it is essentially ‘sodium-free’.

3. How to use Toujeo

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Dose

Based on your life-style and the results of your blood sugar (glucose) tests and your previous insulin usage, your doctor will
- determine how much Toujeo per day you will need and at what time,
- tell you when to check your blood sugar level, and whether you need to carry out urine tests,
- tell you when you may need to inject a higher or lower dose of Toujeo.

Toujeo is a long-acting insulin. Your doctor may tell you to use it in combination with a short-acting insulin or with tablets used to treat high blood sugar levels.

Many factors may influence your blood sugar level. You should know these factors so that you are able to react correctly to changes in your blood sugar level and to prevent it from becoming too high or too low. See the box at the end of this leaflet for further information.

Use in children and adolescents

Toujeo can be used in adolescents and children aged 2 years and above. Use this medicine exactly as your doctor has told you.

Frequency of administration

You need one injection of Toujeo every day, at the same time of the day. OptiSet delivers insulin in increments of 2 units up to a maximum single dose of 40 units.

Method of administration

Toujeo is injected under the skin. Do NOT inject Toujeo in a vein, since this will change its action and may cause hypoglycaemia.

Your doctor will show you in which area of the skin you should inject Toujeo. With each injection, change the puncture site within the particular area of skin that you are using.

How to handle OptiSet

Toujeo comes in cartridges sealed in disposable pen injectors, OptiSet.

Read carefully the "OptiSet Instructions for Use" included in this package leaflet. You must use the pen as described in these Instructions for Use.

A new needle must be attached before each use. Only use needles that have been approved for use with OptiSet.
A safety test must be performed before each injection.

Look at the cartridge before you use the pen. Do not use Toujeo if you notice particles in it. Only use Toujeo if the solution is clear, colourless and waterlike. Do not shake or mix it before use.
To prevent the possible transmission of disease, never share your pen with anyone else. This pen is only for you.

Make sure that neither alcohol nor other disinfectants or other substances contaminate the insulin.

Always use a new pen if you notice that your blood sugar control is unexpectedly getting worse. If you think you may have a problem with OptiSet, please refer to the Questions and Answers section of the attached OptiSet Instructions for Use, or have it checked by your doctor or pharmacist.

Empty pens must not be re-filled and must be properly discarded.

Do not use the OptiSet if it is damaged or not working properly (due to mechanical defects), it has to be discarded and a new OptiSet has to be used.

Insulin mix-ups

You must always check the insulin label before each injection to avoid mix-ups between Toujeo and other insulins.

If you use more Toujeo than you should

- If you have injected too much Toujeo, your blood sugar level may become too low (hypoglycaemia). Check your blood sugar frequently. In general, to prevent hypoglycaemia you must eat more food and monitor your blood sugar. For information on the treatment of hypoglycaemia, see box at the end of this leaflet.

If you forget to use Toujeo

- If you have missed a dose of Toujeo or if you have not injected enough insulin, your blood sugar level may become too high (hyperglycaemia). Check your blood sugar frequently. For information on the treatment of hyperglycaemia, see box at the end of this leaflet.
- Do not take a double dose to make up for a forgotten dose.

If you stop using Toujeo

This could lead to severe hyperglycaemia (very high blood sugar) and ketoacidosis (build-up of acid in the blood because the body is breaking down fat instead of sugar). Do not stop Toujeo without speaking to a doctor, who will tell you what needs to be done.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

If you notice signs of your blood sugar being too low (hypoglycaemia), take action to increase your blood sugar level straight away (see the box at the end of this leaflet). Hypoglycaemia (low blood sugar) can be very serious and is very common with insulin treatment (may affect more than 1 in 10 people). Low blood sugar means that there is not enough sugar in your blood. If your blood sugar level falls too low, you may pass out (become unconscious). Serious hypoglycaemia may cause brain damage and may be life-threatening. For more information, see the box at the end of this leaflet.

Severe allergic reactions (rare, may affect up to 1 in 1,000 people) – the signs may include large-scale skin reactions (rash and itching all over the body), severe swelling of skin or mucous membranes (angiooedema), shortness of breath, a fall in blood pressure with rapid heart beat and
sweating. Severe allergic reactions to insulins may become life-threatening. Tell a doctor straight away if you notice signs of severe allergic reactions.

**Common reported side effects** (may affect up to 1 in 10 people)
- **Skin changes at the injection site**
  If you inject your insulin too often at the same skin site, fatty tissue under the skin at this site may either shrink (lipoatrophy, may affect up to 1 in 100 people) or thicken (lipohypertrophy). The insulin may not work very well. Change the injection site with each injection to help prevent these skin changes.
- **Skin and allergic reactions at the injection site**
  The signs may include redness, unusually intense pain on injection, itching, hives, swelling or inflammation. This can spread around the injection site. Most minor reactions to insulins usually disappear in a few days to a few weeks.

**Rare reported side effect** (may affect up to 1 in 1,000 people)
- **Eye reactions**
  A marked change (improvement or worsening) in your blood sugar control can disturb your vision temporarily. If you have proliferative retinopathy (an eye disease related to diabetes) severe hypoglycaemic attacks may cause temporary loss of vision.
- **General disorders**
  In rare cases, insulin treatment may also cause temporary build-up of water in the body, with swelling in the calves and ankles.

**Very rare reported side-effects** (may affect up to 1 in 10,000 people)
In very rare cases, dysgeusia (taste disorders) and myalgia (muscular pain) can occur.

**Use in children and adolescents**
In general, the side effects in children and adolescents of 18 years of age or less are similar to those seen in adults.
Complaints of injection site reactions (injection site reaction, injection site pain) and skin reactions (rash, urticaria) are reported relatively more frequently in children and adolescents of 18 years of age or less than in adults.
There is no experience in children under 2 years.

**Reporting of side effects**
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. **How to store Toujeo**

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and on the label of the pen after “EXP”. The expiry date refers to the last day of that month.

**Not in-use pens**
Store in a refrigerator (2°C-8°C). Do not freeze or place next to the freezer compartment of your refrigerator or a freezer pack.
Keep the pre-filled pen in the outer carton in order to protect from light.
In-use pens
Pre-filled pens in use or carried as a spare may be stored for a maximum of 4 weeks not above 30°C and away from direct heat or direct light. The pen in use must not be stored in a refrigerator. Do not use it after this time period.

Remove the needle after the injection and store the pen without the needle. Also, be sure to remove the needle before disposing of the pen. Needles must not be re-used.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Toujeo contains

- The active substance is insulin glargine. Each ml of the solution contains 100 units of insulin glargine (equivalent to 3.64 mg).
- The other ingredients are: zinc chloride, metacresol, glycerol, sodium hydroxide (for pH adjustment) (see section 2 “Important information about some of the ingredients of Toujeo”), hydrochloric acid (for pH adjustment) and water for injections.

What Toujeo looks like and contents of the pack

Toujeo OptiSet 100 units/ml solution for injection in a pre-filled pen is a clear colourless solution. Each pen contains 3 ml of solution for injection (equivalent to 300 units). Pack sizes of 1, 3, 4, 5, 6, 8, 9 and 10 pens. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Sanofi-Aventis Deutschland GmbH, D-65926 Frankfurt am Main, Germany.

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder.

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Other source of information
Detailed information on this medicine is available on the European Medicines Agency web site:
http://www.ema.europa.eu/
HYPERGLYCAEMIA AND HYPOGLYCAEMIA

Always carry some sugar (at least 20 grams) with you.
Carry some information with you to show you are diabetic.

HYPERGLYCAEMIA (high blood sugar levels)

If your blood sugar is too high (hyperglycaemia), you may not have injected enough insulin.

Why does hyperglycaemia occur?
Examples include:
- you have not injected your insulin or not injected enough, or if it has become less effective, for example through incorrect storage,
- your insulin pen does not work properly,
- you are doing less exercise than usual, you are under stress (emotional distress, excitement), or you have an injury, operation, infection or fever,
- you are taking or have taken certain other medicines (see section 2, "Other medicines and Toujeo").

Warning symptoms of hyperglycaemia
Thirst, increased need to urinate, tiredness, dry skin, reddening of the face, loss of appetite, low blood pressure, fast heart beat, and glucose and ketone bodies in urine. Stomach pain, fast and deep breathing, sleepiness or even loss of consciousness may be signs of a serious condition (ketoacidosis) resulting from lack of insulin.

What should you do if you experience hyperglycaemia?
Test your blood sugar level and your urine for ketones as soon as any of the above symptoms occur. Severe hyperglycaemia or ketoacidosis must always be treated by a doctor, normally in a hospital.

HYPOGLYCAEMIA (low blood sugar levels)

If your blood sugar level falls too much you may become unconscious. Serious hypoglycaemia may cause a heart attack or brain damage and may be life-threatening. You normally should be able to recognise when your blood sugar is falling too much so that you can take the right actions.

Why does hypoglycaemia occur?
Examples include:
- you inject too much insulin,
- you miss meals or delay them,
- you do not eat enough, or eat food containing less carbohydrate than normal (sugar and substances similar to sugar are called carbohydrates; however, artificial sweeteners are NOT carbohydrates),
- you lose carbohydrates due to vomiting or diarrhoea,
- you drink alcohol, particularly if you are not eating much,
- you are doing more exercise than usual or a different type of physical activity,
- you are recovering from an injury or operation or other stress,
- you are recovering from an illness or from fever,
- you are taking or have stopped taking certain other medicines (see section 2, "Other medicines and Toujeo").
Hypoglycaemia is also more likely to occur if
- you have just begun insulin treatment or changed to another insulin preparation (when changing from your previous basal insulin to Toujeo hypoglycaemia, if it occurs, may be more likely to occur in the morning than at night),
- your blood sugar levels are almost normal or are unstable,
- you change the area of skin where you inject insulin (for example from the thigh to the upper arm),
- you suffer from severe kidney or liver disease, or some other disease such as hypothyroidism.

Warning symptoms of hypoglycaemia

- In your body
Examples of symptoms that tell you that your blood sugar level is falling too much or too fast: sweating, clammy skin, anxiety, fast heart beat, high blood pressure, palpitations and irregular heartbeat. These symptoms often develop before the symptoms of a low sugar level in the brain.

- In your brain
Examples of symptoms that indicate a low sugar level in the brain: headaches, intense hunger, nausea, vomiting, tiredness, sleepiness, sleep disturbances, restlessness, aggressive behaviour, lapses in concentration, impaired reactions, depression, confusion, speech disturbances (sometimes total loss of speech), visual disorders, trembling, paralysis, tingling sensations (paraesthesia), numbness and tingling sensations in the area of the mouth, dizziness, loss of self-control, inability to look after yourself, convulsions, loss of consciousness.

The first symptoms which alert you to hypoglycaemia ("warning symptoms") may change, be weaker or may be missing altogether if
- you are elderly, if you have had diabetes for a long time or if you suffer from a certain type of nervous disease (diabetic autonomic neuropathy),
- you have recently suffered hypoglycaemia (for example the day before) or if it develops slowly,
- you have almost normal or, at least, greatly improved blood sugar levels,
- you have recently changed from an animal insulin to a human insulin such as Toujeo,
- you are taking or have taken certain other medicines (see section 2, "Other medicines and Toujeo").

In such a case, you may develop severe hypoglycaemia (and even faint) before you are aware of the problem. Be familiar with your warning symptoms. If necessary, more frequent blood sugar testing can help to identify mild hypoglycaemic episodes that may otherwise be overlooked. If you are not confident about recognising your warning symptoms, avoid situations (such as driving a car) in which you or others would be put at risk by hypoglycaemia.

What should you do if you experience hypoglycaemia?

1. Do not inject insulin. Immediately take about 10 to 20 g sugar, such as glucose, sugar cubes or a sugar-sweetened beverage. Caution: Artificial sweeteners and foods with artificial sweeteners (such as diet drinks) are of no help in treating hypoglycaemia.
2. Then eat something that has a long-acting effect in raising your blood sugar (such as bread or pasta). Your doctor or nurse should have discussed this with you previously. The recovery of hypoglycaemia may be delayed because Toujeo has a long action.
3. If the hypoglycaemia comes back again take another 10 to 20 g sugar.
4. Speak to a doctor immediately if you are not able to control the hypoglycaemia or if it recurs.
Tell your relatives, friends and close colleagues the following:
If you are not able to swallow or if you are unconscious, you will require an injection of glucose or glucagon (a medicine which increases blood sugar). These injections are justified even if it is not certain that you have hypoglycaemia.

It is advisable to test your blood sugar immediately after taking glucose to check that you really have hypoglycaemia.
Toujeo OPTISET solution for injection in a pre-filled pen. INSTRUCTIONS FOR USE

OptiSet is a pre-filled pen for the injection of insulin. Talk with your doctor, pharmacist or nurse about proper injection technique before using OptiSet.

Read these instructions carefully before using your OptiSet. If you are not able to follow all the instructions completely on your own, use OptiSet only if you have help from a person who is able to follow the instructions. Hold the pen as shown in this leaflet. To ensure that you read the dose correctly, hold the pen horizontally, with the needle on the left and the dosage selector to the right as shown in the illustrations below.

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

You can set doses from 2 to 40 units in steps of 2 units. Each pen contains multiple doses.

If you have any questions about OptiSet or about diabetes, ask your doctor, pharmacist or nurse or call the local representative number on the front of this leaflet.

Keep this leaflet for future reference each time you use OptiSet.

Schematic diagram of the pen

Information for use:
- Name of the insulin is printed on the pen
- Dosage selector can only be turned in one direction

Important information for use of OptiSet:
- Always attach a new needle before each use. Only use needles that are compatible for use with OptiSet.
- Always perform the safety test before each injection (see Step 3).
- If you are using a new OptiSet the initial safety test must be done with the 8 units preset by the manufacturer.
- The dosage selector can only be turned in one direction.
- Never turn the dosage selector (i.e. never change the dose) after injection button has been pulled out.
- 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 OptiSet if it is damaged or if you are not sure that it is working properly.
- Always have a spare OptiSet in case your OptiSet is lost or damaged.
**Step 1. Check the insulin**

**A.** Take off the pen cap.

**B.** Check the label on your OptiSet and insulin reservoir to make sure you have the correct insulin.

**C.** Check the appearance of your insulin. Toujeo is a clear insulin. Do not use this OptiSet if the insulin is cloudy, coloured 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.

Before use of the needle, carefully read the “Instructions for use” accompanying the needles.

Please note: The needles shown are for illustrative purposes only.

**A.** Remove the protective seal from a new needle.

**B.** 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. This ensures that you get an accurate dose by:

- making sure that pen and needle work properly
- removing air bubbles.

If you are using a new OptiSet the initial safety test must be done with the 8 units preset by the manufacturer, otherwise the pen will not function properly.

**A.** Make sure the injection button is pressed in.

**B.** Select the dose for the Safety Test.

- New and unused OptiSet: a dose of 8 units is already preset by the manufacturer for the first safety test.
- In-use OptiSet: select a dose of 2 units by turning the dosage selector forward till the dose arrow points to 2. The dosage selector will only turn in one direction.
C. Pull out the injection button completely in order to load the dose. Never turn the dosage selector after injection button has been pulled out.

D. 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.

E. Hold the pen with the needle pointing upwards.

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

G. 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 OptiSet may be damaged. Do not use this OptiSet.

**Step 4. Select the dose**

You can set the dose in steps of 2 units, from a minimum of 2 units to a maximum of 40 units. If you need a dose greater than 40 units, you should give it as two or more injections.
A. Check if you have enough insulin for your dose.

- The residual insulin scale on the transparent insulin reservoir shows approximately how much insulin remains in the OptiSet. This scale must not be used to set the insulin dose.

- If the black plunger is at the beginning of the coloured bar, then there are approximately 40 units of insulin available.

- If the black plunger is at the end of the coloured bar, then there are approximately 20 units of insulin available.

B. Select your required dose by turning the dose selector forward.

If you turned past your dose,

- and you have not yet pulled the injection button, you can keep turning forward till you reach your dose again,
- and you have already pulled the injection button out, you must discard the dose that has been loaded before you turn the dosage selector again.

Step 5. Load the dose

A. Pull out the injection button completely in order to load the dose.

B. Check if the selected dose is fully loaded. Note that the injection button only goes out as far as the amount of insulin that is left in the reservoir.

- The injection button must be held out under tension during this check.
- The last thick line visible on the injection button shows the amount of insulin loaded. When the injection button is held out only the top part of this thick line can be seen.

- In this example, 12 units are loaded.

  - if you have selected 12 units you can inject your dose.
  - if you have selected more than 12 units then only 12 units of your total insulin dose can be injected with this pen.

In this case what should you do:

- either you can inject what is remaining in the pen and complete your dose with a new OptiSet.
- or use a new OptiSet for your full dose.
Step 6. Inject the dose

A. Use the injection method as instructed by your doctor, pharmacist or nurse.

B. Insert the needle into the skin.

C. Deliver the dose by pressing the injection button in all the way. A clicking sound can be heard, which will stop when the injection button has been pressed in completely.

D. Keep the injection button pressed in and slowly count to 10 before you withdraw the needle from the skin. This ensures that the full dose will be delivered. The pen plunger moves with each dose. The plunger will reach the end of the cartridge when the total of 300 units of insulin has been used.

Step 7. Remove and discard the needle

Always remove the needle after each injection and store OptiSet 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, or if you are giving an injection to another person, special caution must be taken by this person when removing and disposing of the needle. Follow recommended safety measures for removal and disposal of needles (contact your doctor, pharmacist or nurse) in order to reduce the risk of accidental needle injury and transmission of infectious diseases.

B. Dispose of the needle safely, as instructed by your doctor, pharmacist or nurse.

C. Put the pen cap back on, then store the pen until your next injection.

Storage instructions

See Section 5 -How to store Toujeo- of the reverse (insulin) side of this leaflet for OptiSet storage instructions.

If your OptiSet is in cool storage, take it out 1 to 2 hours before you inject to allow it to warm up to room temperature. Cold insulin is more painful to inject.

Discard your used OptiSet as required by your local regulations.
**Maintenance**

Protect your OptiSet from dust and dirt.

You can clean the outside of your OptiSet by wiping it with a damp cloth.

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

It should be handled with care. Avoid situations where OptiSet might be damaged. If you are concerned that your OptiSet may be damaged, discard it and use a new one.
Questions and Answers

<table>
<thead>
<tr>
<th><strong>Wrong dose selected.</strong></th>
<th>• Follow the instructions in Step 4 to select the correct dose.</th>
</tr>
</thead>
</table>
| **Dose has been selected and the injection button has been pulled out and pressed in again without a needle attached.** | 1. Attach a new needle.  
2. Press the injection button completely in and discard the insulin.  
3. Perform the safety test.  
If the safety test is successful OptiSet is ready for use.  
If test is not successful, the pen might be damaged. Use a new OptiSet.  
If in any doubt whether the pen is working correctly use a new OptiSet. |
| **The dosage selector does not turn.** | • You are turning in the wrong direction. The dosage selector can only be turned forward.  
• You are turning forward while the injection button is pulled out. Press the injection button in completely to discard the dose and select again. |
| **The amount indicated on the injection button is higher than the dose selected.** | • Difference is 2 units.  
Discard insulin, then set your dose and check again. If the same error occurs again, OptiSet may be damaged, use a new OptiSet.  
• Difference is more than 2 units  
OptiSet is damaged, use a new OptiSet. |
| **The amount indicated on the injection button is lower than the dose required** | There is not enough insulin in the reservoir. You can do one of the following:  
• inject the amount indicated on the injection button from this OptiSet and then inject the remaining dose using a new OptiSet, or  
• inject the entire dose using a new OptiSet. |
| **The injection button cannot be pressed in.** | 1. Make sure you pulled out the injection button completely.  
2. Attach a new needle.  
3. Press the injection button completely in to discard the insulin.  
4. Perform the safety test. |
| **You don't hear clicking while injecting.** | OptiSet is damaged, use a new OptiSet. |
| **Insulin is leaking from the pen.** | Needle may have been attached imprecisely (e.g. at a slant). Remove needle and replace with a new needle attaching it on straight (see Step 2). Perform the safety test (see Step 3). |
| **Air bubbles are present in the reservoir.** | Small amounts of air may be present in the needle and insulin reservoir during normal use. You must remove this air by performing the safety test (see Step 3).  
The tiny air bubbles in the insulin reservoir that do not move with tapping will not interfere with the injection and dosage. |
| **OptiSet is damaged or is not working properly.** | Do not force it. Do not try to repair or use tools on it. Use a new OptiSet. |
| **OptiSet has been dropped or subjected to impact.** | If in any doubt whether the pen is working correctly use a new OptiSet. |
Package leaflet: Information for the user

Toujeo SoloStar 100 units/ml solution for injection in a pre-filled pen.
Insulin glargine

Read all of this leaflet carefully including the Instructions for Use of Toujeo SoloStar, pre-filled pen, before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet
1. What Toujeo is and what it is used for
2. What you need to know before you use Toujeo
3. How to use Toujeo
4. Possible side effects
5. How to store Toujeo
6. Contents of the pack and other information

1. What Toujeo is and what it is used for

Toujeo contain insulin glargine. This is a modified insulin, very similar to human insulin.

Toujeo is used to treat diabetes mellitus in adults, adolescents and children aged 2 years and above. Diabetes mellitus is a disease where your body does not produce enough insulin to control the level of blood sugar. Insulin glargine has a long and steady blood-sugar-lowering action.

2. What you need to know before you use Toujeo

Do not use Toujeo

- If you are allergic to insulin glargine or to any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Toujeo.
Follow closely the instructions for posology, monitoring (blood and urine tests), diet and physical activity (physical work and exercise), injection technique as discussed with your doctor.

If your blood sugar is too low (hypoglycaemia), follow the guidance for hypoglycaemia (see box at the end of this leaflet).
Travel

Before travelling consult your doctor. You may need to talk about
- the availability of your insulin in the country you are visiting,
- supplies of insulin, syringes etc.,
- correct storage of your insulin while travelling,
- timing of meals and insulin administration while travelling,
- the possible effects of changing to different time zones,
- possible new health risks in the countries to be visited,
- what you should do in emergency situations when you feel unwell or become ill.

Illnesses and injuries

In the following situations, the management of your diabetes may require a lot of care (for example, adjustment to insulin dose, blood and urine tests):
- If you are ill or have a major injury then your blood sugar level may increase (hyperglycaemia).
- If you are not eating enough your blood sugar level may become too low (hypoglycaemia).
In most cases you will need a doctor. Make sure that you contact a doctor early.

If you have type 1 diabetes (insulin dependent diabetes mellitus), do not stop your insulin and continue to get enough carbohydrates. Always tell people who are caring for you or treating you that you require insulin.

Insulin treatment can cause the body to produce antibodies to insulin (substances that act against insulin). However, only very rarely, this will require a change to your insulin dose.

Some patients with long-standing type 2 diabetes mellitus and heart disease or previous stroke who were treated with pioglitazone (oral anti-diabetic medicine used to treat type 2 diabetes mellitus) and insulin experienced the development of heart failure. Inform your doctor as soon as possible if you experience signs of heart failure such as unusual shortness of breath or rapid increase in weight or localised swelling (oedema).

Children

There is no experience with the use of Toujeo in children below the age of 2 years.

Other medicines and Toujeo

Some medicines cause changes in the blood sugar level (decrease, increase or both depending on the situation). In each case, it may be necessary to adjust your insulin dose to avoid blood sugar levels that are either too low or too high. Be careful when you start or stop taking another medicine.

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. Before taking a medicine ask your doctor if it can affect your blood sugar level and what action, if any, you need to take.

Medicines that may cause your blood sugar level to fall (hypoglycaemia) include:
- all other medicines to treat diabetes,
- angiotensin converting enzyme (ACE) inhibitors (used to treat certain heart conditions or high blood pressure),
- disopyramide (used to treat certain heart conditions),
- fluoxetine (used to treat depression),
- fibrates (used to lower high levels of blood lipids),
- monoamine oxidase (MAO) inhibitors (used to treat depression),
- pentoxyfylline, propoxyphene, salicylates (such as acetylsalicylic acid, used to relieve pain and lower fever),
- sulfonamide antibiotics.
Medicines that may cause your blood sugar level to rise (hyperglycaemia) include:
- corticosteroids (such as "cortisone" used to treat inflammation),
- danazol (medicine acting on ovulation),
- diazoxide (used to treat high blood pressure),
- diuretics (used to treat high blood pressure or excessive fluid retention),
- glucagon (pancreas hormone used to treat severe hypoglycaemia),
- isoniazid (used to treat tuberculosis),
- oestrogens and progestogens (such as in the contraceptive pill used for birth control),
- phenothiazine derivatives (used to treat psychiatric disorders),
- somatropin (growth hormone),
- sympathomimetic medicines (such as epinephrine [adrenaline], salbutamol, terbutaline used to treat asthma),
- thyroid hormones (used to treat thyroid gland disorders),
- atypical antipsychotic medicines (such as clozapine, olanzapine),
- protease inhibitors (used to treat HIV).

Your blood sugar level may either rise or fall if you take:
- beta-blockers (used to treat high blood pressure),
- clonidine (used to treat high blood pressure),
- lithium salts (used to treat psychiatric disorders).

Pentamidine (used to treat some infections caused by parasites) may cause hypoglycaemia which may sometimes be followed by hyperglycaemia.

Beta-blockers like other sympatholytic medicines (such as clonidine, guanethidine, and reserpine) may weaken or suppress entirely the first warning symptoms which help you to recognise a hypoglycaemia.

If you are not sure whether you are taking one of those medicines ask your doctor or pharmacist.

Toujeo with alcohol

Your blood sugar levels may either rise or fall if you drink alcohol.

Pregnancy and breast-feeding

Ask your doctor or pharmacist for advice before taking any medicine.

Inform your doctor if you are planning to become pregnant, or if you are already pregnant. Your insulin dose may need to be changed during pregnancy and after giving birth. Particularly careful control of your diabetes, and prevention of hypoglycaemia, is important for the health of your baby.

If you are breast-feeding consult your doctor as you may require adjustments in your insulin doses and your diet.

Driving and using machines

Your ability to concentrate or react may be reduced if:
- you have hypoglycaemia (low blood sugar levels),
- you have hyperglycaemia (high blood sugar levels),
- you have problems with your sight.

Keep this possible problem in mind in all situations where you might put yourself and others at risk (such as driving a car or using machines). You should contact your doctor for advice on driving if:
- you have frequent episodes of hypoglycaemia,
- the first warning symptoms which help you to recognise hypoglycaemia are reduced or absent.
**Important information about some of the ingredients of Toujeo**

This medicine contains less than 1 mmol (23 mg) sodium per dose, i.e. it is essentially ‘sodium-free’.

3. **How to use Toujeo**

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

**Dose**

Based on your life-style and the results of your blood sugar (glucose) tests and your previous insulin usage, your doctor will
- determine how much Toujeo per day you will need and at what time,
- tell you when to check your blood sugar level, and whether you need to carry out urine tests,
- tell you when you may need to inject a higher or lower dose of Toujeo.

Toujeo is a long-acting insulin. Your doctor may tell you to use it in combination with a short-acting insulin or with tablets used to treat high blood sugar levels.

Many factors may influence your blood sugar level. You should know these factors so that you are able to react correctly to changes in your blood sugar level and to prevent it from becoming too high or too low. See the box at the end of this leaflet for further information.

**Use in children and adolescents**

Toujeo can be used in adolescents and children aged 2 years and above. Use this medicine exactly as your doctor has told you.

**Frequency of administration**

You need one injection of Toujeo every day, at the same time of the day.

**Method of administration**

Toujeo is injected under the skin. Do NOT inject Toujeo in a vein, since this will change its action and may cause hypoglycaemia.

Your doctor will show you in which area of the skin you should inject Toujeo. With each injection, change the puncture site within the particular area of skin that you are using.

**How to handle SoloStar**

SoloStar is a pre-filled disposable pen containing insulin glargine.

**Read carefully the "SoloStar Instructions for Use" included in this package leaflet. You must use the pen as described in these Instructions for Use.**

A new needle must be attached before each use. Only use needles that are compatible for use with SoloStar (see “SoloStar Instructions for Use”).
A safety test must be performed before each injection.

Look at the cartridge before you use the pen. Do not use SoloStar if you notice particles in it. Only use SoloStar if the solution is clear, colourless and waterlike. Do not shake or mix it before use.
To prevent the possible transmission of disease, never share your pen with anyone else. This pen is only for you. Make sure that neither alcohol nor other disinfectants or other substances contaminate the insulin.

Always use a new pen if you notice that your blood sugar control is unexpectedly getting worse. If you think you may have a problem with SoloStar, consult your doctor, pharmacist or nurse.

Empty pens must not be re-filled and must be properly discarded.

Do not use SoloStar if it is damaged or not working properly, it has to be discarded and a new SoloStar has to be used.

**Insulin mix-ups**

You must always check the insulin label before each injection to avoid mix-ups between Toujeo and other insulins.

**If you use more Toujeo than you should**

- If you **have injected too much Toujeo**, your blood sugar level may become too low (hypoglycaemia). Check your blood sugar frequently. In general, to prevent hypoglycaemia you must eat more food and monitor your blood sugar. For information on the treatment of hypoglycaemia, see box at the end of this leaflet.

**If you forget to use Toujeo**

- If you **have missed a dose of Toujeo** or if you **have not injected enough insulin**, your blood sugar level may become too high (hyperglycaemia). Check your blood sugar frequently. For information on the treatment of hyperglycaemia, see box at the end of this leaflet.
- Do not take a double dose to make up for a forgotten dose.

**If you stop using Toujeo**

This could lead to severe hyperglycaemia (very high blood sugar) and ketoacidosis (build-up of acid in the blood because the body is breaking down fat instead of sugar). Do not stop Toujeo without speaking to a doctor, who will tell you what needs to be done.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

**4. Possible side effects**

Like all medicines, this medicine can cause side effects, although not everybody gets them.

**If you notice signs of your blood sugar being too low (hypoglycaemia)**, take action to increase your blood sugar level straight away (see the box at the end of this leaflet). Hypoglycaemia (low blood sugar) can be very serious and is very common with insulin treatment (may affect more than 1 in 10 people). Low blood sugar means that there is not enough sugar in your blood. If your blood sugar level falls too low, you may pass out (become unconscious). Serious hypoglycaemia may cause brain damage and may be life-threatening. For more information, see the box at the end of this leaflet.

**Severe allergic reactions** (rare, may affect up to 1 in 1,000 people) – the signs may include large-scale skin reactions (rash and itching all over the body), severe swelling of skin or mucous membranes (angioedema), shortness of breath, a fall in blood pressure with rapid heart beat and sweating. Severe allergic reactions to insulins may become life-threatening. Tell a doctor straight away if you notice signs of severe allergic reactions.
Common reported side effects (may affect up to 1 in 10 people)

• **Skin changes at the injection site**
  If you inject your insulin too often at the same skin site, fatty tissue under the skin at this site may either shrink (lipoatrophy, may affect up to 1 in 100 people) or thicken (lipohypertrophy). The insulin may not work very well. Change the injection site with each injection to help prevent these skin changes.

• **Skin and allergic reactions at the injection site**
  The signs may include reddening, unusually intense pain when injecting, itching, hives, swelling or inflammation. This can spread around the injection site. Most minor reactions to insulins usually disappear in a few days to a few weeks.

Rare reported side effect (may affect up to 1 in 1,000 people)

• **Eye reactions**
  A marked change (improvement or worsening) in your blood sugar control can disturb your vision temporarily. If you have proliferative retinopathy (an eye disease related to diabetes) severe hypoglycaemic attacks may cause temporary loss of vision.

• **General disorders**
  In rare cases, insulin treatment may also cause temporary build-up of water in the body, with swelling in the calves and ankles.

Very rare reported side effects (may affect up to 1 in 10,000 people)

In very rare cases, dysgeusia (taste disorders) and myalgia (muscular pain) can occur.

Use in children and adolescents

In general, the side effects in children and adolescents of 18 years of age or less are similar to those seen in adults.

Complaints of injection site reactions (injection site reaction, injection site pain) and skin reactions (rash, urticaria) are reported relatively more frequently in children and adolescents of 18 years of age or less than in adults.

There is no experience in children under 2 years.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. **How to store Toujeo**

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and on the label of the pen after “EXP”. The expiry date refers to the last day of that month.

**Not in-use pens**

Store in a refrigerator (2°C-8°C). Do not freeze or place next to the freezer compartment or a freezer pack.

Keep the pre-filled pen in the outer carton in order to protect from light.

**In-use pens**

Pre-filled pens in use or carried as a spare may be stored for a maximum of 4 weeks not above 30°C and away from direct heat or direct light. The pen in use must not be stored in the refrigerator. Do not use it after this time period.
Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Toujeo contains

- The active substance is insulin glargine. Each ml of the solution contains 100 units of insulin glargine (equivalent to 3.64 mg).
- The other ingredients are: zinc chloride, metacresol, glycerol, sodium hydroxide (for pH adjustment) (see section 2 “Important information about some of the ingredients of Toujeo”), hydrochloric acid (for pH adjustment) and water for injections.

What Toujeo looks like and contents of the pack

Toujeo SoloStar 100 units/ml solution for injection in a pre-filled pen is a clear and colourless solution. Each pen contains 3 ml of solution for injection (equivalent to 300 units). Pack size of 1, 3, 4, 5, 6, 8, 9 and 10 pre-filled pens. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Sanofi-Aventis Deutschland GmbH, D-65926 Frankfurt am Main, Germany.

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder.

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This leaflet was last revised in

Other source of information
Detailed information on this medicine is available on the European Medicines Agency web site:
http://www.ema.europa.eu/
HYPERGLYCAEMIA AND HYPOGLYCAEMIA

Always carry some sugar (at least 20 grams) with you.
Carry some information with you to show you are diabetic.

HYPERGLYCAEMIA (high blood sugar levels)

If your blood sugar is too high (hyperglycaemia), you may not have injected enough insulin.

Why does hyperglycaemia occur?
Examples include:
- you have not injected your insulin or not injected enough, or if it has become less effective, for example through incorrect storage,
- your insulin pen does not work properly,
- you are doing less exercise than usual, you are under stress (emotional distress, excitement), or you have an injury, operation, infection or fever,
- you are taking or have taken certain other medicines (see section 2, "Other medicines and Toujeo").

Warning symptoms of hyperglycaemia
Thirst, increased need to urinate, tiredness, dry skin, reddening of the face, loss of appetite, low blood pressure, fast heart beat, and glucose and ketone bodies in urine. Stomach pain, fast and deep breathing, sleepiness or even loss of consciousness may be signs of a serious condition (ketoacidosis) resulting from lack of insulin.

What should you do if you experience hyperglycaemia?
Test your blood sugar level and your urine for ketones as soon as any of the above symptoms occur. Severe hyperglycaemia or ketoacidosis must always be treated by a doctor, normally in a hospital.

HYPOGLYCAEMIA (low blood sugar levels)

If your blood sugar level falls too much you may become unconscious. Serious hypoglycaemia may cause a heart attack or brain damage and may be life-threatening. You normally should be able to recognise when your blood sugar is falling too much so that you can take the right actions.

Why does hypoglycaemia occur?
Examples include:
- you inject too much insulin,
- you miss meals or delay them,
- you do not eat enough, or eat food containing less carbohydrate than normal (sugar and substances similar to sugar are called carbohydrates; however, artificial sweeteners are NOT carbohydrates),
- you lose carbohydrates due to vomiting or diarrhoea,
- you drink alcohol, particularly if you are not eating much,
- you are doing more exercise than usual or a different type of physical activity,
- you are recovering from an injury or operation or other stress,
- you are recovering from an illness or from fever,
- you are taking or have stopped taking certain other medicines (see section 2, "Other medicines and Toujeo").
Hypoglycaemia is also more likely to occur if
- you have just begun insulin treatment or changed to another insulin preparation (when changing from your previous basal insulin to Toujeo hypoglycaemia, if it occurs, may be more likely to occur in the morning than at night),
- your blood sugar levels are almost normal or are unstable,
- you change the area of skin where you inject insulin (for example from the thigh to the upper arm),
- you suffer from severe kidney or liver disease, or some other disease such as hypothyroidism.

Warning symptoms of hypoglycaemia

- In your body
Examples of symptoms that tell you that your blood sugar level is falling too much or too fast: sweating, clammy skin, anxiety, fast heart beat, high blood pressure, palpitations and irregular heartbeat. These symptoms often develop before the symptoms of a low sugar level in the brain.

- In your brain
Examples of symptoms that indicate a low sugar level in the brain: headaches, intense hunger, nausea, vomiting, tiredness, sleepiness, sleep disturbances, restlessness, aggressive behaviour, lapses in concentration, impaired reactions, depression, confusion, speech disturbances (sometimes total loss of speech), visual disorders, trembling, paralysis, tingling sensations (paraesthesia), numbness and tingling sensations in the area of the mouth, dizziness, loss of self-control, inability to look after yourself, convulsions, loss of consciousness.

The first symptoms which alert you to hypoglycaemia ("warning symptoms") may change, be weaker or may be missing altogether if
- you are elderly, if you have had diabetes for a long time or if you suffer from a certain type of nervous disease (diabetic autonomic neuropathy),
- you have recently suffered hypoglycaemia (for example the day before) or if it develops slowly,
- you have almost normal or, at least, greatly improved blood sugar levels,
- you have recently changed from an animal insulin to a human insulin such as Toujeo,
- you are taking or have taken certain other medicines (see section 2, "Other medicines and Toujeo").

In such a case, you may develop severe hypoglycaemia (and even faint) before you are aware of the problem. Be familiar with your warning symptoms. If necessary, more frequent blood sugar testing can help to identify mild hypoglycaemic episodes that may otherwise be overlooked. If you are not confident about recognising your warning symptoms, avoid situations (such as driving a car) in which you or others would be put at risk by hypoglycaemia.

What should you do if you experience hypoglycaemia?

1. Do not inject insulin. Immediately take about 10 to 20 g sugar, such as glucose, sugar cubes or a sugar-sweetened beverage. Caution: Artificial sweeteners and foods with artificial sweeteners (such as diet drinks) are of no help in treating hypoglycaemia.
2. Then eat something that has a long-acting effect in raising your blood sugar (such as bread or pasta). Your doctor or nurse should have discussed this with you previously. The recovery of hypoglycaemia may be delayed because Toujeo has a long action.
3. If the hypoglycaemia comes back again take another 10 to 20 g sugar.
4. Speak to a doctor immediately if you are not able to control the hypoglycaemia or if it recurs.
Tell your relatives, friends and close colleagues the following:
If you are not able to swallow or if you are unconscious, you will require an injection of glucose or glucagon (a medicine which increases blood sugar). These injections are justified even if it is not certain that you have hypoglycaemia.

It is advisable to test your blood sugar immediately after taking glucose to check that you really have hypoglycaemia.
SoloStar is a pre-filled pen for the injection of insulin. Your doctor has decided that SoloStar is appropriate for you based on your ability to handle SoloStar. Talk with your doctor, pharmacist or nurse about proper injection technique before using SoloStar.

Read these instructions carefully before using your SoloStar. If you are not able to use SoloStar or follow all the instructions completely on your own, you must use SoloStar only if you have help from a person who is able to follow the instructions completely. Hold the pen as shown in this leaflet. To ensure that you read the dose correctly, hold the pen horizontally, with the needle on the left and the dosage selector to the right as shown in the illustrations below.

You can set doses from 1 to 80 units in steps of 1 unit. Each pen contains multiple doses.

Keep this leaflet for future reference.
If you have any questions about SoloStar or about diabetes, ask your doctor, pharmacist or nurse or call the local representative number on the front of this leaflet.

Important information for use of SoloStar:

- Always attach a new needle before each use. Only use needles that are compatible for use with SoloStar.
- Do not select a dose and/or press the injection button without a needle attached.
- Always perform the safety test before each injection (see Step 3).
- 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.

Step 1. Check the insulin

A. Check the label on your SoloStar to make sure you have the correct insulin. The Toujeo SoloStar is grey with a purple injection button.

B. Take off the pen cap.

C. Check the appearance of your insulin. Toujeo is a clear insulin. Do not use this SoloStar if the insulin is cloudy, coloured 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. Remove the protective seal from a new needle.
B. 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. This 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.

[Image]

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.

[Image]

- 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 doctor, pharmacist or nurse.

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.

The pen plunger moves with each dose. The plunger will reach the end of the cartridge when the total of 300 units of insulin has been used.

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, or if you are giving an injection to another person, special caution must be taken by this person when removing and disposing of the needle. Follow recommended safety measures for removal and disposal of needles (contact your doctor, pharmacist or nurse) in order to reduce the risk of accidental needle injury and transmission of infectious diseases.

B. Dispose of the needle safely, as instructed by your doctor, pharmacist or nurse.

C. Always put the pen cap back on the pen, then store the pen until your next injection.

Storage instructions

See the reverse (insulin) side of this leaflet for 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.

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.

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.