ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Insulin aspart Sanofi 100 units/ml solution for injection in vial
Insulin aspart Sanofi 100 units/ml solution for injection in cartridge
Insulin aspart Sanofi 100 units/ml solution for injection in pre-filled pen

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One ml solution contains 100 units insulin aspart* (equivalent to 3.5 mg).

Insulin aspart Sanofi 100 units/ml solution for injection in vial

Each vial contains 10 ml equivalent to 1,000 units insulin aspart.

Insulin aspart Sanofi 100 units/ml solution for injection in cartridge

Each cartridge contains 3 ml equivalent to 300 units insulin aspart.

Insulin aspart Sanofi 100 units/ml solution for injection in pre-filled pen

Each pre-filled pen contains 3 ml equivalent to 300 units insulin aspart.
Each pre-filled pen delivers 1-80 units in steps of 1 unit.

*produced in *Escherichia coli* by recombinant DNA technology.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection (injection).

Clear, colourless, aqueous solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Insulin aspart Sanofi is indicated for the treatment of diabetes mellitus in adults, adolescents and children aged 1 year and above.

4.2 Posology and method of administration

Posology

The potency of insulin analogues, including insulin aspart, is expressed in units, whereas the potency of human insulin is expressed in international units.

Insulin aspart Sanofi dosing is individual and determined in accordance with the needs of the patient. It should normally be used in combination with intermediate-acting or long-acting insulin.
Moreover, Insulin aspart Sanofi vial can be used for continuous subcutaneous insulin infusion (CSII) in pump systems.

Insulin aspart Sanofi vial can also be used if intravenous administration of insulin aspart, by physicians or other healthcare staff, is applicable.

Blood glucose monitoring and insulin dose adjustments are recommended to achieve optimal glycaemic control.

The individual insulin requirement in adults and children is usually between 0.5 and 1.0 unit/kg/day. In a basal-bolus treatment regimen 50%-70% of this requirement may be provided by Insulin aspart Sanofi and the remainder by intermediate-acting or long-acting insulin.

Adjustment of dose may be necessary if patients undertake increased physical activity, change their usual diet or during concomitant illness.

Transfer from other insulin medicinal products
When transferring from other insulin medicinal products, adjustment of the Insulin aspart Sanofi dose and the dose of the basal insulin may be necessary. Insulin aspart Sanofi has a faster onset and a shorter duration of action than soluble human insulin. When injected subcutaneously into the abdominal wall, the onset of action will occur within 10-20 minutes of injection. The maximum effect is exerted between 1 and 3 hours after the injection. The duration of action is 3 to 5 hours.

Close glucose monitoring is recommended during the transfer and in the initial weeks thereafter (see section 4.4).

Special populations

Elderly (≥ 65 years old)

Insulin aspart Sanofi can be used in elderly patients.
In elderly patients, glucose monitoring should be intensified and the insulin aspart dose adjusted on an individual basis.

Renal impairment

Renal impairment may reduce the patient's insulin requirements.
In patients with renal impairment, glucose monitoring should be intensified and the insulin aspart dose adjusted on an individual basis.

Hepatic impairment

Hepatic impairment may reduce the patient's insulin requirements.
In patients with hepatic impairment, glucose monitoring should be intensified and the insulin aspart dose adjusted on an individual basis.

Paediatric population

Insulin aspart Sanofi can be used in adolescents and children aged 1 year and above in preference to soluble human insulin when a rapid onset of action might be beneficial, for example, in the timing of the injections in relation to meals (see sections 5.1 and 5.2).

The safety and efficacy of Insulin aspart Sanofi in children below 1 year of age have not been established. No data are available.

Method of administration

Insulin aspart is a rapid-acting insulin analogue.
Insulin aspart Sanofi is administered subcutaneously by injection in the upper arms, thighs, buttocks or abdomen. Injection sites should always be rotated within the same region in order to reduce the risk of

lipodystrophy and cutaneous amyloidosis (see section 4.4 and 4.8). Subcutaneous injection in the abdominal wall ensures a faster absorption than other injection sites. Compared to soluble human insulin the faster onset of action of insulin aspart is maintained regardless of the injection site. The duration of action will vary according to the dose, injection site, blood flow, temperature and level of physical activity.

Due to the faster onset of action, insulin aspart should generally be given immediately before a meal. When necessary insulin aspart can be given soon after a meal.

Insulin aspart Sanofi 100 units/ml solution for injection in vial

Continuous subcutaneous insulin infusion (CSII)
Insulin aspart Sanofi may be used for CSII in pump systems suitable for insulin infusion. CSII should be administered in the abdominal wall. Infusion sites should be rotated.
When used with an insulin infusion pump, Insulin aspart Sanofi should not be mixed with any other insulin medicinal products.

Patients using CSII should be comprehensively instructed in the use of the pump system and use the correct reservoir and tubing for the pump (see section 6.6). The infusion set (tubing and cannula) should be changed in accordance with the instructions in the product information supplied with the infusion set.
Patients administering Insulin aspart Sanofi by CSII must have an alternative insulin delivery method available in case of pump system failure.

Intravenous use
If necessary, Insulin aspart Sanofi can be administered intravenously which should be carried out by physicians or other healthcare staff. For intravenous use, infusion systems with Insulin aspart Sanofi 100 units/ml at concentrations from 0.05 unit/ml to 1.0 unit/ml insulin aspart in the infusion fluids: 0.9% sodium chloride solution or 5% glucose, 40 mEq potassium chloride, 0.45% sodium chloride solution or 10% glucose solution using polypropylene infusion bags, are stable at room temperature for 24 hours.
Although stable over time, a certain amount of insulin will be initially adsorbed to the material of the infusion bag. Monitoring of blood glucose is necessary during insulin infusion.

Mixing two types of insulins
Insulin aspart Sanofi should not be mixed with any other insulin medicinal products, including NPH (Neutral Protamine Hagedorn) insulin since respective compatibility studies have not been performed.

Administration with a syringe
Insulin aspart Sanofi vials are for use with insulin syringes with the corresponding unit scale (see section 6.6).

Insulin aspart Sanofi 100 units/ml solution for injection in cartridge

Insulin aspart Sanofi in cartridges is only suitable for subcutaneous injections from a reusable pen. If administration by syringe, intravenous injection or infusion pump is necessary, a vial should be used. Other insulin aspart medicinal products offering such an option should be used. Insulin aspart Sanofi in cartridges is designated to be used in the following pens (see section 6.6):

- JuniorSTAR which delivers 1-30 units of insulin aspart in 0.5 unit dose increments
- Tactipen which delivers 1-60 units of insulin aspart in 1 unit dose increments
- AllStar and AllStar PRO which all deliver 1-80 units of insulin aspart in 1 unit dose increments.

Insulin aspart Sanofi 100 units/ml solution for injection in pre-filled pen

Insulin aspart Sanofi 100 units/ml in pre-filled pen is only suitable for subcutaneous injections. If administration by syringe, intravenous injection or infusion pump is necessary, a vial should be used.

Other insulin aspart medicinal products offering such an option should be used. Insulin aspart Sanofi in pre-filled pen delivers 1-80 units in increments of 1 unit.

Patients must visually verify the dialled units on the dose counter of the pen. Therefore, the requirement for patients to self-inject is that they can read the dose counter on the pen. Patients who are blind or have poor vision must be instructed to always get help/assistance from another person who has good vision and is trained in using the insulin device.

For detailed user instructions, please refer to the package leaflet.

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

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered medicinal product should be clearly recorded.

Patients must be instructed to perform continuous rotation of the injection site to reduce the risk of developing lipodystrophy and cutaneous amyloidosis. There is a potential risk of delayed insulin absorption and worsened glycaemic control following insulin injections at sites with these reactions. A sudden change in the injection site to an unaffected area has been reported to result in hypoglycaemia. Blood glucose monitoring is recommended after the change in the injection site, and dose adjustment of antidiabetic medicinal products may be considered.

Hyperglycaemia

Inadequate dosing or discontinuation of treatment, especially in type 1 diabetes, may lead to hyperglycaemia and diabetic ketoacidosis. Usually the first symptoms of hyperglycaemia develop gradually over a period of hours or days. They include thirst, increased frequency of urination, nausea, vomiting, drowsiness, flushed dry skin, dry mouth, loss of appetite as well as acetone odour of breath. In type 1 diabetes, untreated hyperglycaemic events eventually lead to diabetic ketoacidosis, which is potentially lethal.

Hypoglycaemia

Omission of a meal or unplanned, strenuous physical exercise may lead to hypoglycaemia. Especially in children, care should be taken to match insulin doses (especially in basal-bolus regimens) with food intake, physical activities and current blood glucose level in order to minimise the risk of hypoglycaemia.

Hypoglycaemia may occur if the insulin dose is too high in relation to the insulin requirement. In case of hypoglycaemia or if hypoglycaemia is suspected insulin aspart must not be injected. After stabilisation of patient's blood glucose adjustment of the dose should be considered (see sections 4.8 and 4.9).

Patients whose blood glucose control is greatly improved, e.g. by intensified insulin therapy, may experience a change in their usual warning symptoms of hypoglycaemia, and should be advised accordingly. Usual warning symptoms may disappear in patients with longstanding diabetes.

A consequence of the pharmacodynamics of rapid-acting insulin analogues is that if hypoglycaemia occurs, it may occur earlier after an injection when compared with soluble human insulin.

Since insulin aspart should be administered in immediate relation to a meal, the rapid onset of action should be considered in patients with concomitant diseases or treatment where a delayed absorption of food might be expected.

Concomitant illness, especially infections and feverish conditions, usually increases the patient's insulin requirements. Concomitant diseases in the kidney, liver or affecting the adrenal, pituitary or thyroid gland can require changes in the insulin dose.

When patients are transferred between different types of insulin medicinal products, the early warning symptoms of hypoglycaemia may change or become less pronounced than those experienced with their previous insulin.

Transfer from other insulin medicinal products

Transferring a patient to another type or brand of insulin should be done under strict medical supervision. Changes in strength, brand (manufacturer), type, origin (animal, human insulin or human insulin analogue) and/or method of manufacture (recombinant DNA versus animal source insulin) may result in the need for a change in dose. Patients transferred to Insulin aspart Sanofi from another type of insulin may require an increased number of daily injections or a change in dose from that used with their usual insulin medicinal products. If an adjustment is needed, it may occur with the first dose or during the first few weeks or months.

Injection site reactions

As with any insulin therapy, injection site reactions may occur and include pain, redness, hives, inflammation, bruising, swelling and itching. Continuous rotation of the injection site within a given area reduces the risk of developing these reactions. Reactions usually resolve in a few days to a few weeks. On rare occasions, injection site reactions may require discontinuation of insulin aspart.

Combination of insulin aspart 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 insulin aspart 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.

Avoidance of accidental mix-ups/medication errors

Patients must be instructed to always check the insulin label before each injection to avoid accidental mix-ups between Insulin aspart Sanofi and other insulin medicinal products.

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.

Travel

Before travelling between different time zones, the patient should seek the doctor's advice since this may mean that the patient has to take the insulin and meals at different times.

Sodium

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially "sodium-free".

4.5 Interaction with other medicinal products and other forms of interaction

A number of medicinal products are known to interact with the glucose metabolism.

The following substances may reduce the patient's insulin requirements:
Oral antidiabetic medicinal products, monoamine oxidase inhibitors (MAOI), beta-blockers, angiotensin converting enzyme (ACE) inhibitors, salicylates, anabolic steroids and sulphonamides.

The following substances may increase the patient's insulin requirements:
Oral contraceptives, thiazides, glucocorticoids, thyroid hormones, sympathomimetics, growth hormone and danazol.

Beta-blockers may mask the symptoms of hypoglycaemia.

Octreotide/lanreotide may either increase or decrease the insulin requirement.

Alcohol may intensify or reduce the hypoglycaemic effect of insulin.

4.6 Fertility, pregnancy and lactation

Pregnancy

Insulin aspart Sanofi (insulin aspart) can be used in pregnancy. Data from two randomised controlled clinical trials (322 and 27 exposed pregnancies) do not indicate any adverse reaction of insulin aspart on pregnancy or on the health of the foetus/newborn when compared to human insulin (see section 5.1).

Intensified blood glucose control and monitoring of pregnant women with diabetes (type 1 diabetes, type 2 diabetes or gestational diabetes) are recommended throughout pregnancy and when contemplating pregnancy. Insulin requirements usually fall in the first trimester and increase subsequently during the second and third trimester. After delivery, insulin requirements normally return rapidly to pre-pregnancy values.

Breast-feeding

There are no restrictions on treatment with Insulin aspart Sanofi during breast-feeding. Insulin treatment of the breast-feeding mother presents no risk to the baby. However, the Insulin aspart Sanofi dose may need to be adjusted.

Fertility

Animal reproduction studies have not revealed any differences between insulin aspart and human insulin regarding fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

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

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

4.8 Undesirable effects

Summary of the safety profile

Adverse reactions observed in patients using insulin aspart are mainly due to the pharmacologic effect of insulin.

The most frequently reported adverse reaction during treatment is hypoglycaemia. The frequencies of hypoglycaemia vary with patient population, dose regimens and level of glycaemic control (see section 4.8 Description of selected adverse reactions).

At the beginning of the insulin treatment, refraction anomalies, oedema and injection site reactions (pain, redness, hives, inflammation, bruising, swelling and itching at the injection site) may occur. These reactions are usually of transitory nature. Fast improvement in blood glucose control may be associated with acute painful neuropathy, which is usually reversible. Intensification of insulin therapy with abrupt improvement in glycaemic control may be associated with temporary worsening of diabetic retinopathy, while long-term improved glycaemic control decreases the risk of progression of diabetic retinopathy.

Tabulated list of adverse reactions

Adverse reactions listed below are based on clinical trial data and classified according to System Organ Class. Frequency categories are defined according to the following convention: 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); not known (cannot be estimated from the available data).

MedDRA system organ classes	**Very common**	**Uncommon**	**Rare**	**Very rare**	**Not known**
Immune system disorders		Urticaria, rash, eruptions		Anaphylactic reactions*	
Metabolism and nutrition disorders	Hypoglycaemia*				
Nervous system disorders			Peripheral neuropathy (painful neuropathy)		
Eye disorders		Refraction disorders, diabetic retinopathy			
Skin and subcutaneous tissue disorders		Lipodystrophy*			Cutaneous amyloidosis*
General disorders and administration site conditions		Injection site reactions, oedema			

*See section 4.8 Description of selected adverse reactions

Description of selected adverse reactions

Anaphylactic reactions
The occurrence of generalised hypersensitivity reactions (including generalised skin rash, itching, sweating, gastrointestinal upset, angioneurotic oedema, difficulties in breathing, palpitation and reduction in blood pressure) is very rare but can potentially be life threatening.

Hypoglycaemia
The most frequently reported adverse reaction is hypoglycaemia. It may occur if the insulin dose is too high in relation to the insulin requirement. Severe hypoglycaemia may lead to unconsciousness and/or convulsions and may result in temporary or permanent impairment of brain function or even death. The symptoms of hypoglycaemia usually occur suddenly. They may include cold sweats, cool pale skin, fatigue, nervousness or tremor, anxiousness, unusual tiredness or weakness, confusion, difficulty in concentration, drowsiness, excessive hunger, vision changes, headache, nausea and palpitation.

In clinical trials, the frequency of hypoglycaemia varied with patient population, dose regimens and level of glycaemic control. During clinical trials the overall rates of hypoglycaemia did not differ between patients treated with insulin aspart compared to human insulin.

Skin and subcutaneous tissue disorders
Lipodystrophy (including lipohypertrophy, lipoatrophy) and cutaneous amyloidosis 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 (see section 4.4).

Paediatric population

Based on post-marketing sources and clinical trials with insulin aspart, the frequency, type and severity of adverse reactions observed in the paediatric population do not indicate any differences to the broader experience in the general population.

Other special populations

Based on post-marketing sources and clinical trials with insulin aspart, the frequency, type and severity of adverse reactions observed in the elderly patients and in patients with renal or hepatic impairment do not indicate any differences to the broader experience in the general population.

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

A specific overdose for insulin cannot be defined, however, hypoglycaemia may develop over sequential stages if too high doses relative to the patient's requirement are administered:

- Mild hypoglycaemic episodes can be treated by oral administration of glucose or sugary products. It is therefore recommended that the diabetic patient always carries sugar-containing products.
- Severe hypoglycaemic episodes, where the patient has become unconscious, can be treated with glucagon (0.5 to 1 mg) given intramuscularly or subcutaneously by a trained person, or with glucose given intravenously by physicians or other healthcare staff. Glucose must be given intravenously, if the patient does not respond to glucagon within 10 to 15 minutes. Upon regaining consciousness, administration of oral carbohydrates is recommended for the patient in order to prevent a relapse.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drugs used in diabetes. Insulins and analogues for injection, fast-acting.
ATC code: A10AB05

Insulin aspart Sanofi is a biosimilar medicinal product. Detailed information is available on the website of the European Medicines Agency http://www.ema.europa.eu.

Mechanism of action and pharmacodynamic effects

The blood glucose lowering effect of insulin aspart is due to the facilitated uptake of glucose following binding of insulin to receptors on muscle and fat cells and to the simultaneous inhibition of glucose output from the liver.

Insulin aspart produces a more rapid onset of action compared to soluble human insulin, together with a lower glucose concentration, as assessed within the first four hours after a meal. Insulin aspart has a shorter duration of action compared to soluble human insulin after subcutaneous injection.

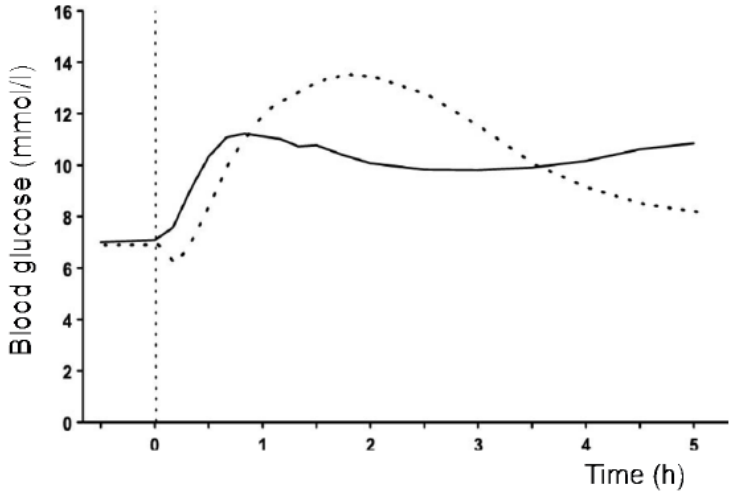

Fig. I. Blood glucose concentrations following a single pre-meal dose of insulin aspart injected immediately before a meal (solid curve) or soluble human insulin administered 30 minutes before a meal (hatched curve) in patients with type 1 diabetes mellitus.

When insulin aspart is injected subcutaneously, the onset of action will occur within 10 to 20 minutes of injection. The maximum effect is exerted between 1 and 3 hours after injection. The duration of action is 3 to 5 hours.

Clinical efficacy

Clinical trials in patients with type 1 diabetes have demonstrated a lower postprandial blood glucose with insulin aspart compared to soluble human insulin (Fig. I). In two long-term open label trials in patients with type 1 diabetes comprising 1070 and 884 patients, respectively, insulin aspart reduced glycated haemoglobin by 0.12 [95% C.I. 0.03; 0.22] percentage points and by 0.15 [95% C.I. 0.05; 0.26] percentage points compared to human insulin; a difference of limited clinical significance.

Clinical trials in patients with type 1 diabetes have demonstrated a reduced risk of nocturnal hypoglycaemia with insulin aspart compared with soluble human insulin. The risk of daytime hypoglycaemia was not significantly increased.

Insulin aspart is equipotent to soluble human insulin on a molar basis.

Special populations

Elderly (≥ 65 years old)
A randomised, double-blind cross-over PK/PD trial comparing insulin aspart with soluble human insulin was performed in elderly patients with type 2 diabetes (19 patients aged 65-83 years, mean age 70 years). The relative differences in the pharmacodynamic properties (GIR_{max},$AUC_{GIR,\ 0\text{-}120\ min}$) between insulin aspart and human insulin in the elderly were similar to those seen in healthy subjects and in younger patients with diabetes.

Paediatric population
A clinical trial comparing preprandial soluble human insulin with postprandial insulin aspart was performed in small children (20 patients aged 2 to less than 6 years, studied for 12 weeks, among those four were younger than 4 years old) and a single dose PK/PD trial was performed in children (6-12 years) and adolescents (13-17 years). The pharmacodynamic profile of insulin aspart in children was similar to that seen in adults.

The efficacy and safety of insulin aspart given as bolus insulin in combination with either insulin detemir or insulin degludec as basal insulin has been studied for up to 12 months, in two randomised controlled clinical trials in adolescents and children aged 1 to less than 18 years (n=712). The trials included 167 children aged 1-5 years, 260 aged 6-11 and 285 aged 12-17. The observed improvements in HbA1c and the safety profiles were comparable between all age groups.

Pregnancy
A clinical trial comparing safety and efficacy of insulin aspart vs. human insulin in the treatment of pregnant women with type 1 diabetes (322 exposed pregnancies (insulin aspart: 157; human insulin: 165) did not indicate any adverse reaction of insulin aspart on pregnancy or on the health of the foetus/newborn.

In addition, the data from a clinical trial including 27 women with gestational diabetes randomised to treatment with insulin aspart vs. human insulin (insulin aspart: 14; human insulin: 13) showed similar safety profiles between treatments.

5.2 Pharmacokinetic properties

Absorption, distribution and elimination

In insulin aspart substitution of amino acid proline with aspartic acid at position B28 reduces the tendency to form hexamers as observed with soluble human insulin. Insulin aspart is therefore more rapidly absorbed from the subcutaneous layer compared to soluble human insulin.

The time to maximum concentration is, on average, half of that for soluble human insulin. A mean maximum plasma concentration of 492±256 pmol/L was reached 40 (interquartile range: 30–40) minutes after a subcutaneous dose of 0.15 unit/kg bodyweight in type 1 diabetic patients. The insulin concentrations returned to baseline about 4 to 6 hours after dose. The absorption rate was somewhat slower in type 2 diabetic patients, resulting in a lower C_{max} (352±240 pmol/L) and later t_{max} (60 (interquartile range: 50–90) minutes). The intra-individual variability in time to maximum concentration is significantly less for insulin aspart than for soluble human insulin, whereas the intra-individual variability in C_{max} for insulin aspart is larger.

Special populations

Elderly (≥ 65 years old)
The relative differences in pharmacokinetic properties between insulin aspart and soluble human insulin in elderly patients (65-83 years, mean age 70 years) with type 2 diabetes were similar to those observed in healthy subjects and in younger patients with diabetes. A decreased absorption rate was

observed in elderly patients, resulting in a later t_{max} (82 (interquartile range: 60-120) minutes), whereas C_{max} was similar to that observed in younger patients with type 2 diabetes and slightly lower than in patients with type 1 diabetes.

Hepatic impairment
A single dose pharmacokinetic study of insulin aspart was performed in 24 subjects with hepatic function ranging from normal to severely impaired. In patients with hepatic impairment, absorption rate was decreased and more variable, resulting in delayed t_{max} from about 50 min in subjects with normal hepatic function to about 85 min in patients with moderate and severe hepatic impairment. AUC, C_{max} and CL/F were similar in patients with reduced hepatic function compared with subjects with normal hepatic function.

Renal impairment
A single dose pharmacokinetic study of insulin aspart in 18 subjects with renal function ranging from normal to severely impaired was performed. No apparent effect of creatinine clearance values on AUC, C_{max}, CL/F and t_{max} of insulin aspart was found. Data were limited in patients with moderate and severe renal impairment. Patients with renal failure necessitating dialysis treatment were not investigated.

Paediatric population
The pharmacokinetic and pharmacodynamic properties of insulin aspart were investigated in children (6–12 years) and adolescents (13–17 years) with type 1 diabetes. Insulin aspart was rapidly absorbed in both age groups, with similar t_{max} as in adults. However, C_{max} differed between the age groups, stressing the importance of the individual titration of insulin aspart.

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 and toxicity to reproduction and development.

In *in vitro* tests, including binding to insulin and IGF-1 receptor sites and effects on cell growth, insulin aspart behaved in a manner that closely resembled human insulin. Studies also demonstrate that the dissociation of binding to the insulin receptor of insulin aspart is equivalent to human insulin.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Phenol
Metacresol
Zinc chloride
Polysorbate 20
Sodium chloride
Hydrochloric acid (for pH adjustment)
Sodium hydroxide (for pH adjustment)
Water for injections

6.2 Incompatibilities

Substances added to Insulin aspart Sanofi may cause degradation of insulin aspart.

<u>Insulin aspart Sanofi 100 units/ml solution for injection in vial</u>

This medicinal product must not be diluted or mixed with other medicinal products, except with infusion fluids as described in section 4.2.

Insulin aspart Sanofi 100 units/ml solution for injection in cartridge and in pre-filled pen

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

It is not recommended to mix Insulin aspart Sanofi with NPH insulin since respective compatibility studies have not been performed.

6.3 Shelf life

Before first use

30 months.

After first use

4 weeks.

6.4 Special precautions for storage

Insulin aspart Sanofi 100 units/ml solution for injection in vial

Before first use
Store in a refrigerator (2°C - 8°C). Do not freeze.
Keep the vial in the outer carton in order to protect from light.

After first use
Store below 30°C. Do not refrigerate. Do not freeze.
Keep the vial in the outer carton in order to protect from light.

Insulin aspart Sanofi 100 units/ml solution for injection in cartridge

Before first use
Store in a refrigerator (2°C - 8°C). Do not freeze.
Keep the cartridge in the outer carton in order to protect from light.

After first use
Store below 30°C. Do not refrigerate. Do not freeze.
Keep the pen cap on the pen in order to protect from light.

Insulin aspart Sanofi 100 units/ml solution for injection in pre-filled pen

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

After first use
Store below 30°C. Do not refrigerate. Do not freeze.
Keep the pen cap on the pen in order to protect from light.

6.5 Nature and contents of container

Insulin aspart Sanofi 100 units/ml solution for injection in vial

Type 1 colourless multi-dose glass vial closed with a flanged cap (aluminium) with tear-off lid (polypropylene) and laminated disk (laminate of isoprene and bromobutyl rubber).
Each vial contains 10 ml of solution.
Pack sizes: 1 or 5 vials.

Not all pack sizes may be marketed.

Insulin aspart Sanofi 100 units/ml solution for injection in cartridge

Type 1 colourless glass cartridge with a grey plunger (bromobutyl rubber) and a flanged cap (aluminium) with a sealing disk (laminate of isoprene and bromobutyl rubber).
Each cartridge contains 3 ml of solution.
Pack sizes: 5 or 10 cartridges
Not all pack sizes may be marketed.

Insulin aspart Sanofi 100 units/ml solution for injection in pre-filled pen

Type 1 colourless glass cartridge with a grey plunger (bromobutyl rubber) and a flanged cap (aluminium) with a sealing disk (laminate of isoprene and bromobutyl rubber) sealed in a disposable pen injector (SoloStar).
Each pre-filled pen contains 3 ml of solution.
Pack sizes: 1, 5 or 10 pre-filled pens.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

The Insulin aspart Sanofi solution should be inspected before use. This medicinal product should not be used if the solution is not clear, colourless and aqueous.

Insulin aspart Sanofi which has been frozen must not be used.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Insulin aspart Sanofi 100 units/ml solution for injection in vial

To prevent the possible transmission of disease, each vial must be used by one patient only, even if the needle is changed.

Insulin aspart Sanofi vial may be used in an infusion pump system (CSII) subcutaneously as described in section 4.2. Tubings in which the inner surface materials are made of polyethylene have been evaluated and found compatible with pump use.

Insulin aspart Sanofi vial may be used intravenously as described in section 4.2.

A new needle should always be used for each injection.

Syringes and needles are not included in the pack.

Insulin aspart Sanofi 100 units/ml solution for injection in cartridge

To prevent the possible transmission of disease, each cartridge must be used by one patient only, even if the needle on the delivery device is changed.

Insulin aspart Sanofi in cartridges are to be used with JuniorSTAR, Tactipen, AllStar or AllStar PRO pens as recommended (see section 4.2 and 4.4).

The pen with the inserted cartridge should not be stored with the needle attached.

A new needle should always be used for each injection.

The manufacturer's instructions with each individual pen must be followed for loading the cartridge, attaching the needle and administering the insulin injection

Insulin aspart Sanofi 100 units/ml solution for injection in pre-filled pen

To prevent the possible transmission of disease, each pen must be used by one patient only, even if the needle is changed.

The pre-filled pen should not be stored with the needle attached.

A new needle should always be used for each injection.

Needles are not included in the pack.

7. MARKETING AUTHORISATION HOLDER

Sanofi Winthrop Industrie
82 avenue Raspail
94250 Gentilly
France

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1447/001
EU/1/20/1447/002
EU/1/20/1447/003
EU/1/20/1447/004
EU/1/20/1447/005
EU/1/20/1447/006
EU/1/20/1447/007

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 25 June 2020

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
Brüningstrasse 50
Industriepark Höchst
65926 Frankfurt am Main
Germany

Name and address of the manufacturers responsible for batch release

Sanofi-Aventis Deutschland GmbH
Brüningstrasse 50
Industriepark Höchst
65926 Frankfurt am Main
Germany

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 (PSURs)**

The requirements for submission of PSURs 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 marketing authorisation holder (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.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (10 ml VIAL)

1. NAME OF THE MEDICINAL PRODUCT

Insulin aspart Sanofi 100 units/ml solution for injection in vial
insulin aspart

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One ml solution contains 100 units insulin aspart (equivalent to 3.5 mg).
Each vial contains 10 ml equivalent to 1,000 units insulin aspart.

3. LIST OF EXCIPIENTS

Excipients: phenol, metacresol, zinc chloride, polysorbate 20, sodium chloride, hydrochloric acid and sodium hydroxide (for pH adjustment), water for injections. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
1 x 10 ml
5 x 10 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous or intravenous 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

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Before first use:
Store in a refrigerator.
Do not freeze.

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

After first use:
Store below 30°C for a maximum of 4 weeks.
Do not refrigerate.
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 Winthrop Industrie
82 avenue Raspail
94250 Gentilly
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1447/006 1 vial
EU/1/20/1447/007 5 vials

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Insulin aspart Sanofi 100

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL (10 ml VIAL)

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

Insulin aspart Sanofi 100 units/ml injection
insulin aspart
Subcutaneous or intravenous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

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

Insulin aspart Sanofi 100 units/ml solution for injection in cartridge
insulin aspart

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One ml solution contains 100 units (equivalent to 3.5 mg) insulin aspart.
Each cartridge contains 3 ml equivalent to 300 units insulin aspart.

3. LIST OF EXCIPIENTS

Excipients: phenol, metacresol, zinc chloride, polysorbate 20, sodium chloride, hydrochloric acid and sodium hydroxide (for pH adjustment), water for injections. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
5 x 3 ml
10 x 3 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Use the cartridges only with the pens: AllStar, AllStar PRO, JuniorSTAR, Tactipen.
Not all of 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

For single patient use only.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Before first use:
Store in a refrigerator
Do not freeze.
Keep the cartridge in the outer carton in order to protect from light.

After first use:
Store below 30°C for a maximum of 4 weeks.
Do not refrigerate.
Keep the pen cap on the pen 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 Winthrop Industrie
82 avenue Raspail
94250 Gentilly
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1447/004 5 cartridges
EU/1/20/1447/005 10 cartridges

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Insulin aspart Sanofi 100

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL (CARTRIDGE)

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

Insulin aspart Sanofi 100 units/ml solution for injection
insulin aspart
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)

1. NAME OF THE MEDICINAL PRODUCT

Insulin aspart Sanofi 100 units/ml solution for injection in pre-filled pen
insulin aspart

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One ml solution contains 100 units (equivalent to 3.5 mg) insulin aspart.
Each pre-filled pen contains 3 ml equivalent to 300 units insulin aspart.

3. LIST OF EXCIPIENTS

Excipients: phenol, metacresol, zinc chloride, polysorbate 20, sodium chloride, hydrochloric acid and sodium hydroxide (for pH adjustment), water for injections. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection in pre-filled pen SoloStar
1 pen of 3 ml
5 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

Always use a new needle for each injection.
For single patient use only

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Before first use:
Store in a refrigerator.
Do not freeze.
Keep the pre-filled pen in the outer carton in order to protect from light.

After first use:
Store below 30°C for a maximum of 4 weeks.
Do not refrigerate.
Keep the pen cap on the pen 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 Winthrop Industrie
82 avenue Raspail
94250 Gentilly
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1447/001 1 pen
EU/1/20/1447/002 5 pens
EU/1/20/1447/003 10 pens

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Insulin aspart 100 SoloStar

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PEN LABEL (PRE-FILLED PEN)

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

Insulin aspart Sanofi 100 units/ml solution for injection
insulin aspart
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

SoloStar

B. PACKAGE LEAFLET

Package leaflet: information for the user

Insulin aspart Sanofi 100 units/ml solution for injection in vial
insulin aspart

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, nurse or pharmacist.
- 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, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

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

1. What Insulin aspart Sanofi is and what it is used for

Insulin aspart Sanofi is a modern insulin (insulin analogue) with a rapid-acting effect. Modern insulin products are improved versions of human insulin.

Insulin aspart Sanofi is used to reduce the high blood sugar level in adults, adolescents and children aged 1 year and above with diabetes mellitus (diabetes). Diabetes is a disease where your body does not produce enough insulin to control the level of your blood sugar. Treatment with insulin aspart helps to prevent complications from your diabetes.

Insulin aspart will start to lower your blood sugar 10–20 minutes after you inject it, a maximum effect occurs between 1 and 3 hours after the injection and the effect lasts for 3–5 hours. Due to this short action insulin aspart should normally be taken in combination with intermediate-acting or long-acting insulin preparations. Moreover, Insulin aspart Sanofi can be used for continuous subcutaneous infusion in a pump system.

2. What you need to know before you use Insulin aspart Sanofi

Do not use Insulin aspart Sanofi
- If you are allergic to insulin aspart, or any of the other ingredients of this medicine (listed in "Contents of the pack and other information" section 6).
- If you suspect hypoglycaemia (low blood sugar) is starting (see "Summary of serious and very common side effects" in section 4).
- If the protective cap is loose or missing. Each vial has a protective, aluminium cap with tear-off lid. If it is not in perfect condition when you get the vial, return the vial to your supplier.
- If it has not been stored correctly or been frozen (see "How to store Insulin aspart Sanofi" in section 5).
- If the insulin does not appear clear and colourless.

If any of these applies, do not use Insulin aspart Sanofi. Talk with your doctor, nurse or pharmacist for advice.

Before using Insulin aspart Sanofi
- Check the label to make sure it is the right type of insulin.
- Remove the protective cap.
- Always use a new needle for each injection to prevent contamination.
- Needles and syringes must not be shared.

Warnings and precautions
Record the brand name ("Insulin aspart Sanofi") and Lot number (included on the outer carton and label of each vial) of the medicine you are using and provide this information when reporting any side effects.

Skin changes at the injection site
The injection site should be rotated to prevent skin changes such as lumps under the skin. The insulin may not work very well if you inject into a lumpy area (see "How to use Insulin aspart Sanofi"). Contact your doctor if you are currently injecting into a lumpy area before you start injecting in a different area. Your doctor may tell you to check your blood sugar more closely, and to adjust your insulin or your other antidiabetic medications dose.

Some conditions and activities can affect your need for insulin. Consult your doctor:
- If you have trouble with your kidneys or liver, or with your adrenal, pituitary or thyroid glands.
- If you exercise more than usual or if you want to change your usual diet, as this may affect your blood sugar level.
- If you are ill, carry on taking your insulin and consult your doctor.
- If you are going abroad, travelling over time zones may affect your insulin needs and the timing of your injections.

Children and adolescents
Do not give this medicine to children below 1 year of age since no clinical trials have been carried out in children below the age of 1 year.

Other medicines and Insulin aspart Sanofi
Tell your doctor, nurse or pharmacist if you are taking, have recently taken or might take any other medicines.
Some medicines affect your blood sugar level and this may mean that your insulin dose has to change. Listed below are the most common medicines which may affect your insulin treatment.

Your blood sugar level may fall (hypoglycaemia) if you take:
- Other medicines for the treatment of diabetes
- Monoamine oxidase inhibitors (MAOI) (used to treat depression)
- Beta–blockers (used to treat high blood pressure)
- Angiotensin converting enzyme (ACE) inhibitors (used to treat certain heart conditions or high blood pressure)
- Salicylates (used to relieve pain and lower fever)
- Anabolic steroids (such as testosterone)
- Sulphonamides (used to treat infections).

Your blood sugar level may rise (hyperglycaemia) if you take:
- Oral contraceptives (birth control pills)
- Thiazides (used to treat high blood pressure or excessive fluid retention)
- Glucocorticoids (such as 'cortisone' used to treat inflammation)
- Thyroid hormones (used to treat thyroid gland disorders)
- Sympathomimetics (such as epinephrine [adrenaline], or salbutamol, terbutaline used to treat asthma)

- Growth hormone (medicine for stimulation of skeletal and somatic growth and pronounced influence on the body's metabolic processes)
- Danazol (medicine acting on ovulation).

Octreotide and lanreotide (used for treatment of acromegaly, a rare hormonal disorder that usually occurs in middle-aged adults, caused by the pituitary gland producing excess growth hormone) may either increase or decrease your blood sugar level.

Beta-blockers (used to treat high blood pressure) may weaken or suppress entirely the first warning symptoms which help you to recognise low blood sugar.

Pioglitazone (tablets used for the treatment of type 2 diabetes)
Some patients with long-standing type 2 diabetes and heart disease or previous stroke who were treated with pioglitazone 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).

If you have taken any of the medicines listed here, tell your doctor, nurse or pharmacist.

Insulin aspart and alcohol
If you drink alcohol, your need for insulin may change as your blood sugar level may either rise or fall. Careful monitoring is recommended.

Pregnancy and breast-feeding
If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before using this medicine. Insulin aspart can be used during pregnancy. Your insulin dose may need to be changed during pregnancy and after delivery. Careful control of your diabetes, particularly prevention of hypoglycaemia, is important for the health of your baby.

There are no restrictions on treatment with insulin aspart during breast-feeding.

Ask your doctor, nurse or pharmacist for advice before using this medicine while pregnant or breast-feeding.

Driving and using machines
Please ask your doctor whether you can drive a car or use a machine:
- If you have frequent hypoglycaemia.
- If you find it hard to recognise hypoglycaemia.

If your blood sugar is low or high, your concentration and ability to react might be affected and therefore also your ability to drive or use a machine. Bear in mind that you could endanger yourself or others.

Insulin aspart Sanofi has a rapid onset of effect therefore if hypoglycaemia occurs, you may experience it earlier after an injection when compared to soluble human insulin.

Insulin aspart Sanofi contains sodium
This medicine contains less than 1 mmol (23 mg) sodium per dose, that is to say essentially "sodium-free".

3. How to use Insulin aspart Sanofi

Dose and when to use your insulin
Always use your insulin and adjust your dose exactly as your doctor has told you. Check with your doctor, nurse or pharmacist if you are not sure.

Insulin aspart is generally used immediately before a meal. Eat a meal or snack within 10 minutes of the injection to avoid low blood sugar. When necessary, insulin aspart can be given soon after a meal (see "How and where to inject" below for information).

Do not change your insulin unless your doctor tells you to. If your doctor has switched you from one type or brand of insulin to another, your dose may have to be adjusted by your doctor.

Use in children and adolescents
Insulin aspart can be used in adolescents and children aged 1 year and above instead of soluble human insulin when a rapid onset of effect is preferred. For example, when it is difficult to dose the child in relation to meals.

Use in special patient groups
If you have reduced kidney or liver function, or if you are above 65 years of age, you need to check your blood sugar more regularly and discuss changes in your insulin dose with your doctor.

How to use and where to inject
Insulin aspart Sanofi is for injection under the skin (subcutaneously) or for continuous subcutaneous infusion in a pump system. Administration in a pump system will require a comprehensive instruction by your healthcare professional. You must never inject yourself directly into a vein (intravenously) or muscle (intramuscularly). If necessary, Insulin aspart Sanofi can be given directly into a vein but this must only be done by physicians or other healthcare staff.

With each injection, change the injection site within the particular area of skin that you use. This may reduce the risk of developing lumps or skin pitting (see section 4 "Possible side effects"). The best places to give yourself an injection are: the front of your waist (abdomen), the upper arm or the front of your thighs. The insulin will work more quickly if you inject into the front of your waist (abdomen). You should always measure your blood sugar regularly.

How to handle Insulin aspart Sanofi in vial
1. Draw into the syringe the same amount of air as the dose of insulin you are going to inject. Inject the air into the vial.
2. Turn the vial and syringe upside down and draw the correct insulin dose into the syringe. Pull the needle out of the vial. Then expel the air from the syringe and check that the dose is correct.

How to inject Insulin aspart Sanofi
- Inject the insulin under the skin. Use the injection technique advised by your doctor or nurse.
- Keep the needle under your skin for at least 6 seconds to make sure you have injected all the insulin.
- Discard the needle after each injection.

For use in an infusion pump system
Insulin aspart Sanofi should never be mixed with any other insulin when used in a pump.
Follow the instructions and recommendations from your doctor regarding the use of Insulin aspart Sanofi in a pump. Before use of Insulin aspart Sanofi in the pump system, you must have received a comprehensive instruction in the use and information about any actions to be taken in case of illness, too high or too low blood sugar or failure of the pump system.
- Before inserting the needle, use soap and water to clean your hands and the skin where the needle is inserted to avoid any infection at the infusion site.
- When you fill a new reservoir, be certain not to leave large air bubbles in either the syringe or the tubing.
- Changing of the infusion set (tubing and needle) must be done according to the instructions in the product information supplied with the infusion set.

To get the benefit of insulin infusion, and to detect possible malfunction of the insulin pump, it is recommended that you measure your blood sugar level regularly.

What to do in case of pump system failure
You should always have an alternative delivery method for your insulin available for injection under the skin in case of pump system failure.

If you use more insulin than you should
If you use too much insulin your blood sugar gets too low (hypoglycaemia) (see “Summary of serious and very common side effects” in section 4).

If you forget to use your insulin
If you forget to use your insulin your blood sugar may get too high (hyperglycaemia) (see “Effects from diabetes” in section 4).

If you stop using your insulin
Do not stop using your insulin without speaking with a doctor, who will tell you what needs to be done. This could lead to very high blood sugar (severe hyperglycaemia) and ketoacidosis (see “Effects from diabetes” in section 4).

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

4. Possible side effects

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

Summary of serious and very common side effects

Low blood sugar (hypoglycaemia) is a very common side effect. It may affect more than 1 in 10 people.

Low blood sugar may occur if you:
- Inject too much insulin.
- Eat too little or miss a meal.
- Exercise more than usual.
- Drink alcohol (see "Insulin aspart and alcohol” in section 2).

Signs of low blood sugar: Cold sweat; cool pale skin; headache; rapid heartbeat; feeling sick; feeling very hungry; temporary changes in vision; drowsiness; unusual tiredness and weakness; nervousness or tremor; feeling anxious; feeling confused; difficulty in concentrating.

Severe low blood sugar can lead to unconsciousness. If prolonged severe low blood sugar is not treated, it can cause brain damage (temporary or permanent) and even death. You may recover more quickly from unconsciousness with an injection of the hormone glucagon by someone who knows how to use it. If you are given glucagon you will need glucose or a sugar snack as soon as you are conscious. If you do not respond to glucagon treatment, you will have to be treated in a hospital.

What to do if you experience low blood sugar:
- If you experience low blood sugar, eat glucose tablets or another high sugar snack (e.g. sweets, biscuits, fruit juice). Measure your blood sugar if possible and rest. Always carry glucose tablets or high sugar snacks with you, just in case.
- When symptoms of low blood sugar have disappeared or when blood sugar level is stabilised, continue insulin treatment as usual.
- If you have such a low blood sugar that it makes you pass out, if you have had need for injection of glucagon, or if you have experienced many incidents of low blood sugar, talk with a doctor. The amount or timing of insulin, food or exercise may need to be adjusted.

Tell relevant people that you have diabetes and what the consequences may be, including the risk of passing out (become unconscious) due to low blood sugar. Let them know that if you pass out, they must turn you on your side and get medical help straight away. They must not give you any food or drink due to risk of suffocation.

Serious allergic reactions to Insulin aspart Sanofi or one of its ingredients (called a systemic allergic reaction) is a very rare side effect but can potentially be life-threatening. It may affect up to 1 in 10,000 people.

Seek medical advice immediately:
- If signs of allergy spread to other parts of your body.
- If you suddenly feel unwell, and you: start sweating; start being sick (vomiting); have difficulty in breathing; have a rapid heartbeat; feel dizzy.

If you notice any of these signs, seek medical advice immediately.

Other side effects

Skin changes at the injection site: If you inject insulin too often at the same place, the fatty tissue under the skin at the injection site may shrink (lipoatrophy) or thicken (lipohypertrophy) (may affect up to 1 in 100 people). Lumps under the skin may also be caused by build-up of a protein called amyloid (cutaneous amyloidosis; how often this occurs is not known). The insulin may not work very well if you inject into a lumpy area. Change the injection site with each injection to help prevent these skin changes. If you notice your skin pitting or thickening at the injection site, tell your doctor or nurse. These reactions can become more severe, or they may change the absorption of your insulin, if you inject in such a site.

Uncommon (may affect up to 1 in 100 people)

Signs of allergy: Local allergic reactions (pain, redness, hives, inflammation, bruising, swelling and itching) at the injection site may occur. These usually disappear after a few weeks of using your insulin. If they do not disappear, or if they spread throughout your body, talk to your doctor immediately (see also “Serious allergic reactions” above).

Vision problems: When you first start your insulin treatment, it may disturb your vision, but the disturbance is usually temporary.

Swollen joints: When you start using insulin, water retention may cause swelling around your ankles and other joints. Normally this soon disappears. If not, talk to your doctor.

Diabetic retinopathy (an eye disease related to diabetes which can lead to loss of vision): If you have diabetic retinopathy and your blood sugar level improves very fast, the retinopathy may get worse. Ask your doctor about this.

Rare side effects (may affect up to 1 in 1,000 people).

Painful neuropathy (pain due to nerve damage): If your blood sugar level improves very fast, you may get nerve-related pain. This is called acute painful neuropathy and is usually transient.

Reporting of side effects
If you get any side effects, talk to your doctor, nurse 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.

Effects from diabetes

High blood sugar (hyperglycaemia)

High blood sugar may occur if you:
- Have not injected enough insulin.
- Forget to inject your insulin or stop using insulin.
- Repeatedly inject less insulin than you need.
- Get an infection and/or a fever.
- Eat more than usual.
- Exercise less than usual.

Warning signs of high blood sugar:
The warning signs appear gradually. They include: increased urination; feeling thirsty; losing your appetite; feeling sick (nausea or vomiting); feeling drowsy or tired; flushed; dry skin; dry mouth and a fruity (acetone) smell of the breath.

What to do if you experience high blood sugar
- If you get any of the above signs: test your blood sugar level, test your urine for ketones if you can, then seek medical advice immediately.
- These may be signs of a very serious condition called diabetic ketoacidosis (build-up of acid in the blood because the body is breaking down fat instead of sugar). If you do not treat it, this could lead to diabetic coma and eventually death.

5. How to store Insulin aspart Sanofi

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 label and carton. The expiry date refers to the last day of that month.

Before the first use: store your Insulin aspart Sanofi in a refrigerator (2°C - 8°C). Do not freeze. Keep the vial in the outer carton in order to protect from light.

After first opening: Keep your Insulin aspart Sanofi vial that you are using at room temperature (below 30°C) for a maximum of 4 weeks. Do not keep the vial that you are using in the fridge or freeze. Keep the vial in the outer carton in order to protect from light.

Do not use Insulin aspart Sanofi vial if the solution is coloured or it has solid pieces in it. You must use it **only** if it looks like water. Check this each time you inject yourself.

Discard the needle after each injection.

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 to protect the environment.

6. Contents of the pack and other information

What Insulin aspart Sanofi contains
- The active substance is insulin aspart. One ml of the solution contains 100 units of insulin aspart (equivalent to 3.5 mg). Each vial contains 10 ml of solution for injection, equivalent to 1,000 units of insulin aspart.
- The other ingredients are: phenol, metacresol, zinc chloride, polysorbate 20, sodium chloride, hydrochloric acid/sodium hydroxide and water for injections. Sodium hydroxide or hydrochloric

acid may have been used to adjust the acidity (see “Insulin aspart Sanofi contains sodium” in section 2).

What Insulin aspart Sanofi looks like and contents of the pack
Insulin aspart Sanofi solution for injection (injection) is a clear, colourless solution.
Each vial contains 10 ml.

Insulin aspart Sanofi in vial comes in a pack of 1 or 5 vials. Not all pack sizes may be marketed.

Marketing Authorisation Holder
Sanofi Winthrop Industrie, 82 avenue Raspail, 94250 Gentilly, France

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/

Package leaflet: information for the user

Insulin aspart Sanofi 100 units/ml solution for injection in cartridge
insulin aspart

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, nurse or pharmacist.
- 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, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

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

1. What Insulin aspart Sanofi is and what it is used for

Insulin aspart Sanofi is a modern insulin (insulin analogue) with a rapid-acting effect. Modern insulin products are improved versions of human insulin.

Insulin aspart Sanofi is used to reduce the high blood sugar level in adults, adolescents and children aged 1 year and above with diabetes mellitus (diabetes). Diabetes is a disease where your body does not produce enough insulin to control the level of your blood sugar. Treatment with insulin aspart helps to prevent complications from your diabetes.

Insulin aspart will start to lower your blood sugar 10–20 minutes after you inject it, a maximum effect occurs between 1 and 3 hours after the injection and the effect lasts for 3–5 hours. Due to this short action insulin aspart should normally be taken in combination with intermediate-acting or long-acting insulin preparations.

2. What you need to know before you use Insulin aspart Sanofi

Do not use Insulin aspart Sanofi
- If you are allergic to insulin aspart, or any of the other ingredients of this medicine (listed in section 6).
- If you suspect hypoglycaemia (low blood sugar) is starting (see “Summary of serious and very common side effects” in section 4).
- If the cartridge or the device containing the cartridge is dropped, damaged or crushed.
- If it has not been stored correctly or been frozen (see “How to store Insulin aspart Sanofi” in section 5).
- If the insulin does not appear clear and colourless.

If any of these applies, do not use Insulin aspart Sanofi. Talk with your doctor, nurse or pharmacist for advice.

Before using Insulin aspart Sanofi
- Check the label to make sure it is the right type of insulin.
- Always check the cartridge, including the rubber plunger at the bottom of the cartridge. Do not use it if any damage is seen or if the rubber plunger has been drawn above the white label band at the bottom of the cartridge. This could be a result of leakage of insulin. If you suspect the cartridge is damaged, take it back to your supplier. See your pen manual for further instructions.
- Always use a new needle for each injection to prevent contamination.
- Needles and pens must not be shared.
- Insulin aspart Sanofi is only suitable for injecting under the skin using a reusable pen. Speak to your doctor if you need to inject your insulin by another method.

Warnings and precautions

Record the brand name ("Insulin aspart Sanofi") and Lot number (included on the outer cartons and labels of each cartridge) of the medicine you are using and provide this information when reporting any side effects.

Skin changes at the injection site
The injection site should be rotated to prevent skin changes such as lumps under the skin. The insulin may not work very well if you inject into a lumpy area (see How to use Insulin aspart Sanofi). Contact your doctor if you are currently injecting into a lumpy area before you start injecting in a different area. Your doctor may tell you to check your blood sugar more closely, and to adjust your insulin or your other antidiabetic medications dose.

Some conditions and activities can affect your need for insulin. Consult your doctor:
- If you have trouble with your kidneys or liver, or with your adrenal, pituitary or thyroid glands.
- If you exercise more than usual or if you want to change your usual diet, as this may affect your blood sugar level.
- If you are ill, carry on taking your insulin and consult your doctor.
- If you are going abroad, travelling over time zones may affect your insulin needs and the timing of your injections.

Children and adolescents
Do not give this medicine to children below 1 year of age since no clinical trials have been carried out in children below the age of 1 year.

Other medicines and Insulin aspart Sanofi
Tell your doctor, nurse or pharmacist if you are taking, have recently taken or might take any other medicines.
Some medicines affect your blood sugar level and this may mean that your insulin dose has to change. Listed below are the most common medicines which may affect your insulin treatment.

Your blood sugar level may fall (hypoglycaemia) if you take:
- Other medicines for the treatment of diabetes
- Monoamine oxidase inhibitors (MAOI) (used to treat depression)
- Beta–blockers (used to treat high blood pressure)
- Angiotensin converting enzyme (ACE) inhibitors (used to treat certain heart conditions or high blood pressure)
- Salicylates (used to relieve pain and lower fever)
- Anabolic steroids (such as testosterone)
- Sulphonamides (used to treat infections).

Your blood sugar level may rise (hyperglycaemia) if you take:
- Oral contraceptives (birth control pills)
- Thiazides (used to treat high blood pressure or excessive fluid retention)

- Glucocorticoids (such as 'cortisone' used to treat inflammation)
- Thyroid hormones (used to treat thyroid gland disorders)
- Sympathomimetics (such as epinephrine [adrenaline], or salbutamol, terbutaline used to treat asthma)
- Growth hormone (medicine for stimulation of skeletal and somatic growth and pronounced influence on the body's metabolic processes)
- Danazol (medicine acting on ovulation).

Octreotide and lanreotide (used for treatment of acromegaly, a rare hormonal disorder that usually occurs in middle–aged adults, caused by the pituitary gland producing excess growth hormone) may either increase or decrease your blood sugar level.

Beta–blockers (used to treat high blood pressure) may weaken or suppress entirely the first warning symptoms which help you to recognise low blood sugar.

Pioglitazone (tablets used for the treatment of type 2 diabetes)
Some patients with long–standing type 2 diabetes and heart disease or previous stroke who were treated with pioglitazone 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).

If you have taken any of the medicines listed here, tell your doctor, nurse or pharmacist.

Insulin aspart and alcohol
If you drink alcohol, your need for insulin may change as your blood sugar level may either rise or fall. Careful monitoring is recommended.

Pregnancy and breast-feeding
If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before using this medicine. Insulin aspart can be used during pregnancy. Your insulin dose may need to be changed during pregnancy and after delivery. Careful control of your diabetes, particularly prevention of hypoglycaemia, is important for the health of your baby.

There are no restrictions on treatment with insulin aspart during breast-feeding.

Ask your doctor, nurse or pharmacist for advice before using this medicine while pregnant or breast-feeding.

Driving and using machines
Please ask your doctor whether you can drive a car or use a machine:
- If you have frequent hypoglycaemia.
- If you find it hard to recognise hypoglycaemia.

If your blood sugar is low or high, your concentration and ability to react might be affected and therefore also your ability to drive or use a machine. Bear in mind that you could endanger yourself or others.

Insulin aspart Sanofi has a rapid onset of effect therefore if hypoglycaemia occurs, you may experience it earlier after an injection when compared to soluble human insulin.

Insulin aspart Sanofi contains sodium
This medicine contains less than 1 mmol (23 mg) sodium per dose, that to say essentially "sodium-free".

3. How to use Insulin aspart Sanofi

Dose and when to use your insulin
Always use your insulin and adjust your dose exactly as your doctor has told you. Check with your doctor, nurse or pharmacist if you are not sure.

Insulin aspart is generally used immediately before a meal. Eat a meal or snack within 10 minutes of the injection to avoid low blood sugar. When necessary, insulin aspart can be given soon after a meal (see "How and where to inject below for information").

Do not change your insulin unless your doctor tells you to. If your doctor has switched you from one type or brand of insulin to another, your dose may have to be adjusted by your doctor.

Use in children and adolescents
Insulin aspart can be used in adolescents and children aged 1 year and above instead of soluble human insulin when a rapid onset of effect is preferred. For example, when it is difficult to dose the child in relation to meals.

Use in special patient groups
If you have reduced kidney or liver function, or if you are above 65 years of age, you need to check your blood sugar more regularly and discuss changes in your insulin dose with your doctor.

How to use and where to inject
Insulin aspart Sanofi is for injection under the skin (subcutaneously). You must never inject yourself directly into a vein (intravenously) or muscle (intramuscularly). Insulin aspart Sanofi 100 units/ml in cartridges is only suitable for injecting under the skin using a reusable pen. Speak to your doctor if you need to inject your insulin by another method.

With each injection, change the injection site within the particular area of skin that you use. This may reduce the risk of developing lumps or skin pitting (see section 4 "Possible side effects"). The best places to give yourself an injection are: the front of your waist (abdomen), the upper arm or the front of your thighs. The insulin will work more quickly if you inject into the front of your waist (abdomen). You should always measure your blood sugar regularly.

- To ensure you get the accurate dose, the Insulin aspart Sanofi cartridges are to be used only with the following pens:
  - JuniorSTAR which delivers doses in steps of 0.5 units
  - Tactipen, AllStar and AllStar PRO which deliver doses in steps of 1 unit.

  Not all of these pens may be marketed in your country.
- Always carry a spare cartridge in case it is lost or damaged.

How to inject Insulin aspart Sanofi
- Inject the insulin under the skin. Use the injection technique advised by your doctor or nurse and as described in your pen manual.
- Keep the needle under your skin for at least 10 seconds. Keep the dose button held in until the needle has been released from the skin. This will ensure you get your full dose.
- Remove and discard the needle after each injection. Do not store Insulin aspart Sanofi with the needle attached. Otherwise the liquid may leak out which can cause inaccurate dosing.
- Always use a new needle for each injection. This helps stop blocked needles, contamination and infection.

If you use more insulin than you should
If you use too much insulin your blood sugar gets too low (hypoglycaemia) (see "Summary of serious and very common side effects" in section 4).

If you forget to use your insulin
If you forget to use your insulin your blood sugar may get too high (hyperglycaemia) (see "Effects from diabetes" in section 4).

If you stop using your insulin
Do not stop using your insulin without speaking with a doctor, who will tell you what needs to be done. This could lead to very high blood sugar (severe hyperglycaemia) and ketoacidosis (see "Effects from diabetes" in section 4).

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

4. Possible side effects

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

Summary of serious and very common side effects

Low blood sugar (hypoglycaemia) is a very common side effect. It may affect more than 1 in 10 people.

Low blood sugar may occur if you:
- Inject too much insulin.
- Eat too little or miss a meal.
- Exercise more than usual.
- Drink alcohol (see "Insulin aspart and alcohol" in section 2).

Signs of low blood sugar:
Cold sweat; cool pale skin; headache; rapid heartbeat; feeling sick; feeling very hungry; temporary changes in vision; drowsiness; unusual tiredness and weakness; nervousness or tremor; feeling anxious; feeling confused; difficulty in concentrating.

Severe low blood sugar can lead to unconsciousness. If prolonged severe low blood sugar is not treated, it can cause brain damage (temporary or permanent) and even death. You may recover more quickly from unconsciousness with an injection of the hormone glucagon by someone who knows how to use it. If you are given glucagon you will need glucose or a sugar snack as soon as you are conscious. If you do not respond to glucagon treatment, you will have to be treated in a hospital.

What to do if you experience low blood sugar:
- If you experience low blood sugar, eat glucose tablets or another high sugar snack (e.g. sweets, biscuits, fruit juice). Measure your blood sugar if possible and rest. Always carry glucose tablets or high sugar snacks with you, just in case.
- When symptoms of low blood sugar have disappeared or when blood sugar level is stabilised, continue insulin treatment as usual.
- If you have such a low blood sugar that it makes you pass out, if you have had need for injection of glucagon, or if you have experienced many incidents of low blood sugar, talk with a doctor. The amount or timing of insulin, food or exercise may need to be adjusted.

Tell relevant people that you have diabetes and what the consequences may be, including the risk of passing out (become unconscious) due to low blood sugar. Let them know that if you pass out, they must turn you on your side and get medical help straight away. They must not give you any food or drink due to risk of suffocation.

Serious allergic reactions to Insulin aspart Sanofi or one of its ingredients (called a systemic allergic reaction) is a very rare side effect but can potentially be life threatening. It may affect up to 1 in 10,000 people.

Seek medical advice immediately:
- If signs of allergy spread to other parts of your body.
- If you suddenly feel unwell, and you: start sweating; start being sick (vomiting); have difficulty in breathing; have a rapid heartbeat; feel dizzy.

If you notice any of these signs, seek medical advice immediately.

Other side effects

Skin changes at the injection site: If you inject insulin too often at the same place, the fatty tissue under the skin at the injection site may shrink (lipoatrophy) or thicken (lipohypertrophy) *(*may affect up to 1 in 100 people*)*. Lumps under the skin may also be caused by build-up of a protein called amyloid (cutaneous amyloidosis; how often this occurs is not known). The insulin may not work very well if you inject into a lumpy area. Change the injection site with each injection to help prevent these skin changes. If you notice your skin pitting or thickening at the injection site, tell your doctor or nurse. These reactions can become more severe, or they may change the absorption of your insulin, if you inject in such a site.

Uncommon (may affect up to 1 in 100 people)

Signs of allergy: Local allergic reactions (pain, redness, hives, inflammation, bruising, swelling and itching) at the injection site may occur. These usually disappear after a few weeks of using your insulin. If they do not disappear, or if they spread throughout your body, talk to your doctor immediately (see also "Serious allergic reactions" above).

Vision problems: When you first start your insulin treatment, it may disturb your vision, but the disturbance is usually temporary.

Swollen joints: When you start using insulin, water retention may cause swelling around your ankles and other joints. Normally this soon disappears. If not, talk to your doctor.

Diabetic retinopathy (an eye disease related to diabetes which can lead to loss of vision): If you have diabetic retinopathy and your blood sugar level improves very fast, the retinopathy may get worse. Ask your doctor about this.

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

Painful neuropathy (pain due to nerve damage): If your blood sugar level improves very fast, you may get nerve related pain This is called acute painful neuropathy and is usually transient.

Reporting of side effects
If you get any side effects, talk to your doctor, nurse 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.

Effects from diabetes

High blood sugar (hyperglycaemia)

High blood sugar may occur if you:
- Have not injected enough insulin.
- Forget to inject your insulin or stop using insulin.
- Repeatedly inject less insulin than you need.
- Get an infection and/or a fever.
- Eat more than usual.
- Exercise less than usual.

Warning signs of high blood sugar:
The warning signs appear gradually. They include: increased urination; feeling thirsty; losing your appetite; feeling sick (nausea or vomiting); feeling drowsy or tired; flushed; dry skin; dry mouth and a fruity (acetone) smell of the breath.

What to do if you experience high blood sugar
- If you get any of the above signs: test your blood sugar level, test your urine for ketones if you can, then seek medical advice immediately.
- These may be signs of a very serious condition called diabetic ketoacidosis (build-up of acid in the blood because the body is breaking down fat instead of sugar). If you do not treat it, this could lead to diabetic coma and eventually death.

5. How to store Insulin aspart Sanofi

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 label and carton. The expiry date refers to the last day of that month.

Before the first use store your Insulin aspart Sanofi in a refrigerator (2°C – 8°C). Do not freeze. Keep the cartridge in the outer carton in order to protect from light.

Keep your cartridge in use at room temperature (below 30°C) for a maximum of 4 weeks. Do not put it near heat or in the sun. Do not keep your pen with the inserted cartridge you are using in the fridge. The pen with the inserted cartridge should not be stored with the needle attached. Keep the pen cap on the pen to protect it from light.

Do not use Insulin aspart Sanofi, if it is coloured or it has solid pieces in it. You must use it **only** if it looks like water. Check this each time you inject yourself.

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 to protect the environment.

6. Contents of the pack and other information

What Insulin aspart Sanofi contains
- The active substance is insulin aspart. One ml of the solution contains 100 units (equivalent to 3.5 mg) of insulin aspart. Each cartridge contains 3 ml of solution for injection, equivalent to 300 units of insulin aspart.
- The other ingredients are: phenol, metacresol, zinc chloride, polysorbate 20, sodium chloride, hydrochloric acid/sodium hydroxide and water for injections. Sodium hydroxide or hydrochloric acid may have been used to adjust the acidity (see “Insulin aspart Sanofi contains sodium” in section 2).

What Insulin aspart Sanofi looks like and contents of the pack
Insulin aspart Sanofi, solution for injection is a clear, colourless solution. Each cartridge contains 3 ml.

Do not refill the cartridge. Once empty, it must be disposed of.

If you are treated with Insulin aspart Sanofi in cartridge and another insulin in cartridge, you should use the insulin delivery systems recommended by each manufacturer, one for each type of insulin.

The Insulin aspart Sanofi cartridges come in a pack of 5 or 10 cartridges.
Not all pack sizes may be marketed.

Marketing Authorisation Holder
Sanofi Winthrop Industrie, 82 avenue Raspail, 94250 Gentilly, France

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/

Package leaflet: information for the user

Insulin aspart Sanofi 100 units/ml solution for injection in pre-filled pen
insulin aspart

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, nurse or pharmacist.
- 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, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Insulin aspart Sanofi is and what it is used for
2. What you need to know before you use Insulin aspart Sanofi
3. How to use Insulin aspart Sanofi
4. Possible side effects
5. How to store Insulin aspart Sanofi
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1. What Insulin aspart Sanofi is and what it is used for

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Insulin aspart will start to lower your blood sugar 10–20 minutes after you inject it, a maximum effect occurs between 1 and 3 hours after the injection and the effect lasts for 3–5 hours. Due to this short action insulin aspart should normally be taken in combination with intermediate-acting or long-acting insulin preparations.

2. What you need to know before you use Insulin aspart Sanofi

Do not use Insulin aspart Sanofi
- If you are allergic to insulin aspart, or any of the other ingredients of this medicine (listed in section 6).
- If you suspect hypoglycaemia (low blood sugar) is starting (see “Summary of serious and very common side effects” in section 4)
- If the pre-filled pen is dropped, damaged or crushed.
- If it has not been stored correctly or been frozen (see “How to store Insulin aspart Sanofi” in section 5).
- If the insulin does not appear clear and colourless.

If any of these applies, do not use Insulin aspart Sanofi. Talk with your doctor, nurse or pharmacist for advice.

Before using Insulin aspart Sanofi
- Check the label to make sure it is the right type of insulin.
- Always use a new needle for each injection to prevent contamination.
- Needles and the pre-filled pen must not be shared.
- Insulin aspart Sanofi is only suitable for injecting under the skin. Speak to your doctor if you need to inject your insulin by another method.

Warnings and precautions
Record the brand name ("Insulin aspart Sanofi") and Lot number (included on the outer cartons and labels of each pre-filled pen) of the medicine you are using and provide this information when reporting any side effects.

Skin changes at the injection site
The injection site should be rotated to prevent skin changes such as lumps under the skin. The insulin may not work very well if you inject into a lumpy area (see How to use Insulin aspart Sanofi). Contact your doctor if you are currently injecting into a lumpy area before you start injecting in a different area. Your doctor may tell you to check your blood sugar more closely, and to adjust your insulin or your other antidiabetic medications dose.

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- If you have trouble with your kidneys or liver, or with your adrenal, pituitary or thyroid glands.
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Your blood sugar level may rise (hyperglycaemia) if you take:
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- Thiazides (used to treat high blood pressure or excessive fluid retention)
- Glucocorticoids (such as 'cortisone' used to treat inflammation)
- Thyroid hormones (used to treat thyroid gland disorders)
- Sympathomimetics (such as epinephrine [adrenaline], or salbutamol, terbutaline used to treat asthma)
- Growth hormone (medicine for stimulation of skeletal and somatic growth and pronounced influence on the body's metabolic processes)
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Beta–blockers (used to treat high blood pressure) may weaken or suppress entirely the first warning symptoms which help you to recognise low blood sugar.

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Some patients with long–standing type 2 diabetes and heart disease or previous stroke who were treated with pioglitazone 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).

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Insulin aspart and alcohol
If you drink alcohol, your need for insulin may change as your blood sugar level may either rise or fall. Careful monitoring is recommended.

Pregnancy and breast-feeding
If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before using this medicine. Insulin aspart can be used during pregnancy. Your insulin dose may need to be changed during pregnancy and after delivery. Careful control of your diabetes, particularly prevention of hypoglycaemia, is important for the health of your baby.

There are no restrictions on treatment with insulin aspart during breast-feeding.

Ask your doctor, nurse or pharmacist for advice before using this medicine while pregnant or breast-feeding.

Driving and using machines
Please ask your doctor whether you can drive a car or use a machine:
- If you have frequent hypoglycaemia.
- If you find it hard to recognise hypoglycaemia.

If your blood sugar is low or high, your concentration and ability to react might be affected and therefore also your ability to drive or use a machine. Bear in mind that you could endanger yourself or others.

Insulin aspart Sanofi has a rapid onset of effect therefore if hypoglycaemia occurs, you may experience it earlier after an injection when compared to soluble human insulin.

Insulin aspart Sanofi contains sodium
This medicine contains less than 1 mmol (23 mg) sodium per dose, that to say essentially “sodium-free”.

3. How to use Insulin aspart Sanofi

Dose and when to use your insulin
Always use your insulin and adjust your dose exactly as your doctor has told you. Check with your doctor, nurse or pharmacist if you are not sure.

Insulin aspart is generally used immediately before a meal. Eat a meal or snack within 10 minutes of the injection to avoid low blood sugar. When necessary, insulin aspart can be given soon after a meal (see “How and where to inject below for information”).

Do not change your insulin unless your doctor tells you to. If your doctor has switched you from one type or brand of insulin to another, your dose may have to be adjusted by your doctor.

Use in children and adolescents
Insulin aspart can be used in adolescents and children aged 1 year and above instead of soluble human insulin when a rapid onset of effect is preferred. For example, when it is difficult to dose the child in relation to meals.

Use in special patient groups
If you have reduced kidney or liver function, or if you are above 65 years of age, you need to check your blood sugar more regularly and discuss changes in your insulin dose with your doctor.

How to use and where to inject
Insulin aspart Sanofi is for injection under the skin (subcutaneously). You must never inject yourself directly into a vein (intravenously) or muscle (intramuscularly). Insulin aspart Sanofi is only suitable for injecting under the skin. Speak to your doctor if you need to inject your insulin by another method.

With each injection, change the injection site within the particular area of skin that you use. This may reduce the risk of developing lumps or skin pitting (see section 4 "Possible side effects"). The best places to give yourself an injection are: the front of your waist (abdomen), the upper arm or the front of your thighs. The insulin will work more quickly if you inject into the front of your waist (abdomen). You should always measure your blood sugar regularly.

How to handle Insulin aspart Sanofi SoloStar pre-filled pen
Insulin aspart Sanofi SoloStar is a pre-filled disposable pen containing insulin aspart. Each SoloStar pen delivers 1-80 units in increments of 1 unit.

Read carefully the instructions for use included in this package leaflet. You must use the pen as described in the Instructions for Use.

Always ensure you use the correct pen before you inject your insulin.

If you use more insulin than you should
If you use too much insulin your blood sugar gets too low (hypoglycaemia) (see "Summary of serious and very common side effects" in section 4).

If you forget to use your insulin
If you forget to use your insulin your blood sugar may get too high (hyperglycaemia) (see "Effects from diabetes" in section 4).

If you stop using your insulin
Do not stop using your insulin without speaking with a doctor, who will tell you what needs to be done. This could lead to very high blood sugar (severe hyperglycaemia) and ketoacidosis (see "Effects from diabetes" in section 4).

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

4. Possible side effects

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

Summary of serious and very common side effects

Low blood sugar (hypoglycaemia) is a very common side effect. It may affect more than 1 in 10 people.

Low blood sugar may occur if you:
- Inject too much insulin.
- Eat too little or miss a meal.
- Exercise more than usual.
- Drink alcohol (see "Insulin aspart and alcohol" in section 2).

Signs of low blood sugar:
Cold sweat; cool pale skin; headache; rapid heartbeat; feeling sick; feeling very hungry; temporary changes in vision; drowsiness; unusual tiredness and weakness; nervousness or tremor; feeling anxious; feeling confused; difficulty in concentrating.

Severe low blood sugar can lead to unconsciousness. If prolonged severe low blood sugar is not treated, it can cause brain damage (temporary or permanent) and even death. You may recover more quickly from unconsciousness with an injection of the hormone glucagon by someone who knows how to use it. If you are given glucagon you will need glucose or a sugar snack as soon as you are conscious. If you do not respond to glucagon treatment, you will have to be treated in a hospital.

What to do if you experience low blood sugar:
- If you experience low blood sugar, eat glucose tablets or another high sugar snack (e.g. sweets, biscuits, fruit juice). Measure your blood sugar if possible and rest. Always carry glucose tablets or high sugar snacks with you, just in case.
- When symptoms of low blood sugar have disappeared or when blood sugar level is stabilised, continue insulin treatment as usual.
- If you have such a low blood sugar that it makes you pass out, if you have had need for injection of glucagon, or if you have experienced many incidents of low blood sugar, talk with a doctor. The amount or timing of insulin, food or exercise may need to be adjusted.

Tell relevant people that you have diabetes and what the consequences may be, including the risk of passing out (become unconscious) due to low blood sugar. Let them know that if you pass out, they must turn you on your side and get medical help straight away. They must not give you any food or drink due to risk of suffocation.

Serious allergic reactions to Insulin aspart Sanofi or one of its ingredients (called a systemic allergic reaction) is a very rare side effect but can potentially be life threatening. It may affect up to 1 in 10,000 people.

Seek medical advice immediately:
- If signs of allergy spread to other parts of your body.
- If you suddenly feel unwell, and you: start sweating; start being sick (vomiting); have difficulty in breathing; have a rapid heartbeat; feel dizzy.

If you notice any of these signs, seek medical advice immediately.

Other side effects

Skin changes at the injection site: If you inject insulin too often at the same place, the fatty tissue under the skin at the injection site may shrink (lipoatrophy) or thicken (lipohypertrophy) *(*may affect up to 1 in 100 people*)*. Lumps under the skin may also be caused by build-up of a protein called amyloid (cutaneous amyloidosis; how often this occurs is not known). The insulin may not work very well if you inject into a lumpy area. Change the injection site with each injection to help prevent these skin changes. If you notice your skin pitting or thickening at the injection site, tell your doctor or nurse. These reactions can become more severe, or they may change the absorption of your insulin, if you inject in such a site

Uncommon (may affect up to 1 in 100 people)

Signs of allergy: Local allergic reactions (pain, redness, hives, inflammation, bruising, swelling and itching) at the injection site may occur. These usually disappear after a few weeks of using your insulin. If they do not disappear, or if they spread throughout your body, talk to your doctor immediately (see also "Serious allergic reactions above).

Vision problems: When you first start your insulin treatment, it may disturb your vision, but the disturbance is usually temporary.

Swollen joints: When you start using insulin, water retention may cause swelling around your ankles and other joints. Normally this soon disappears. If not, talk to your doctor.

Diabetic retinopathy (an eye disease related to diabetes which can lead to loss of vision): If you have diabetic retinopathy and your blood sugar level improves very fast, the retinopathy may get worse. Ask your doctor about this.

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

Painful neuropathy (pain due to nerve damage): If your blood sugar level improves very fast, you may get nerve related pain. This is called acute painful neuropathy and is usually transient.

Reporting of side effects
If you get any side effects, talk to your doctor, nurse 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.

Effects from diabetes

High blood sugar (hyperglycaemia)

High blood sugar may occur if you:
- Have not injected enough insulin.
- Forget to inject your insulin or stop using insulin.
- Repeatedly inject less insulin than you need.
- Get an infection and/or a fever.
- Eat more than usual.
- Exercise less than usual.

Warning signs of high blood sugar:
The warning signs appear gradually. They include: increased urination; feeling thirsty; losing your appetite; feeling sick (nausea or vomiting); feeling drowsy or tired; flushed; dry skin; dry mouth and a fruity (acetone) smell of the breath.

What to do if you experience high blood sugar
- If you get any of the above signs: test your blood sugar level, test your urine for ketones if you can, then seek medical advice immediately.
- These may be signs of a very serious condition called diabetic ketoacidosis (build-up of acid in the blood because the body is breaking down fat instead of sugar). If you do not treat it, this could lead to diabetic coma and eventually death.

5. How to store Insulin aspart Sanofi

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 label and carton. The expiry date refers to the last day of that month.

Before the first use store your Insulin aspart Sanofi in a refrigerator (2°C – 8°C). Do not freeze. Keep the pre-filled pen in the outer carton in order to protect from light.

Keep your Insulin aspart Sanofi pre-filled pen in use at room temperature (below 30°C) for a maximum of 4 weeks. Do not keep the pre-filled pen that you are using in the fridge. The pre-filled pen should not be stored with the needle attached. Always keep the cap on the pre-filled pen when you are not using it in order to protect from light.

Do not use Insulin aspart Sanofi pre-filled pen if the solution is coloured or it has solid pieces in it. You must use it **only** if it looks like water. Check this each time you inject yourself.

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 to protect the environment.

6. Contents of the pack and other information

What Insulin aspart Sanofi contains

- The active substance is insulin aspart. One ml of the solution contains 100 units (equivalent to 3.5 mg) of insulin aspart. Each pre-filled pen (SoloStar) contains 3 ml of solution for injection, equivalent to 300 units of insulin aspart. Each pre-filled pen (SoloStar) delivers 1-80 units in steps of 1 unit.
- The other ingredients are: phenol, metacresol, zinc chloride, polysorbate 20, sodium chloride, hydrochloric acid/sodium hydroxide and water for injections. Sodium hydroxide or hydrochloric acid may have been used to adjust the acidity (see “Insulin aspart Sanofi contains sodium” in section 2).

What Insulin aspart Sanofi looks like and contents of the pack
Insulin aspart Sanofi solution for injection is a clear, colourless solution. Each pre-filled pen (SoloStar) contains 3 ml.

Only use needles that are compatible for use with Insulin aspart Sanofi.

Insulin aspart Sanofi in pre-filled pen (SoloStar) comes in a pack of 1, 5 or 10 pre-filled pens. Not all pack sizes may be marketed.

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Manufacturer
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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/

Insulin aspart Sanofi solution for injection in pre-filled pen (SoloStar)
INSTRUCTIONS FOR USE

Read this first

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.
- **Never re-use needles.** If you do you might not get your dose (underdosing) or get too much (overdosing) as the needle could block.

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 package leaflet information and instructions before using your pen. If you do not follow all of these instructions, you may get too much or too little insulin.

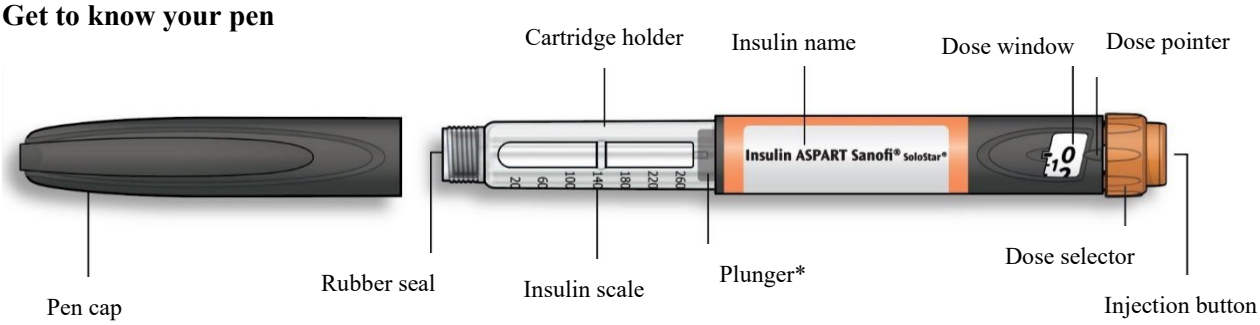
Need help?

If you have any questions about your pen or about diabetes, ask your doctor, pharmacist or nurse or contact the local representative of the Marketing Authorization Holder mentioned 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 (see **Throwing your pen away**).

Get to know your pen



* You will not see the plunger until you have injected a few doses.

STEP 1: Check your pen

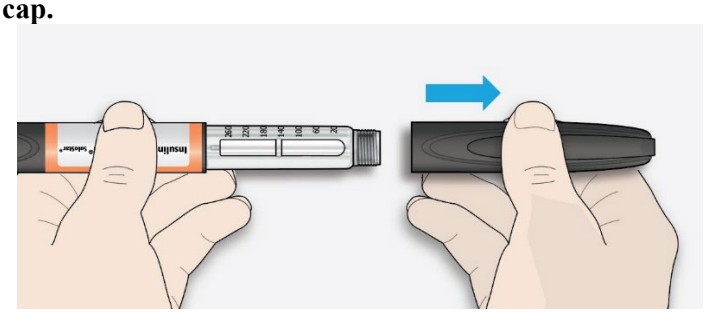
- Take a new pen out of the fridge at least 1 hour before you inject. Cold insulin is more painful to inject.

1A Check the name and expiry 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 expiry date.

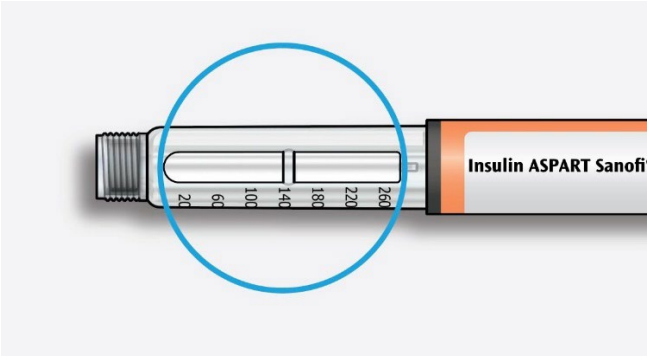


1B Pull off the pen cap.



1C Check that the insulin is clear.

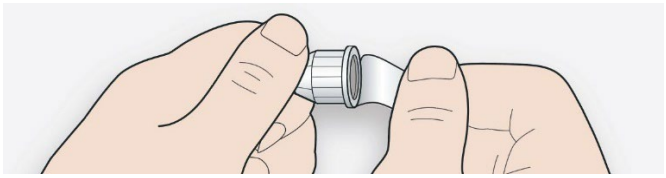
- Do not use the pen if the insulin looks cloudy, coloured or contains particles.



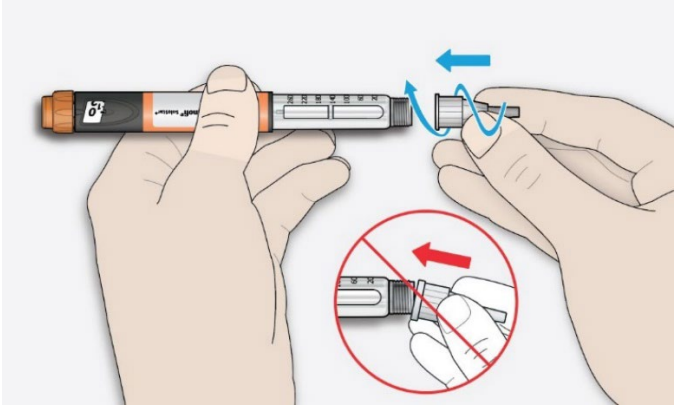
STEP 2: Attach a new needle

- 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 Insulin aspart Sanofi.

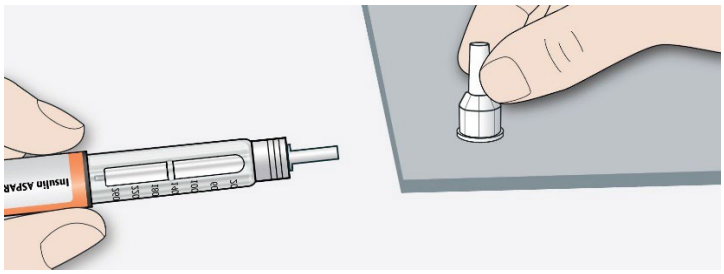
2A Take a new needle and peel off the protective seal.



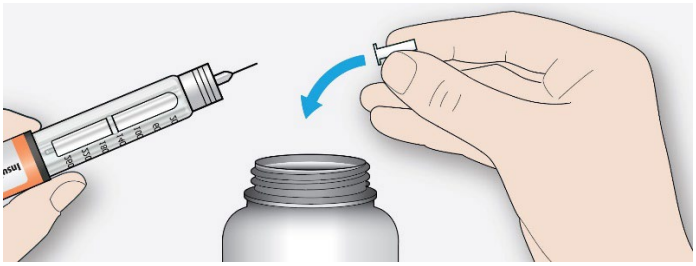
2B Keep the needle straight and screw it onto the pen until fixed. Do not overtighten.



2C Pull off the outer needle cap. Keep this for later.



2D Pull off the inner needle cap and throw away.



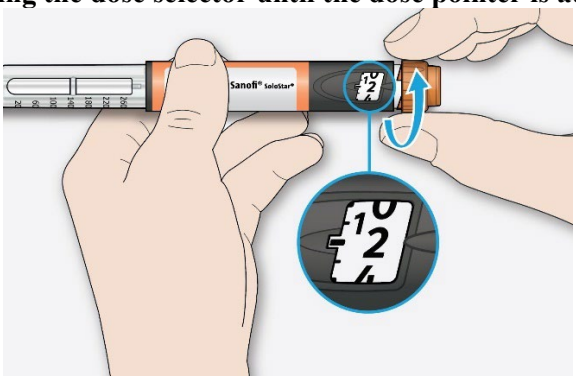
Handling needles

- Take care when handling needles – this is to prevent needle injury and cross-infection.

STEP 3: Do a safety test

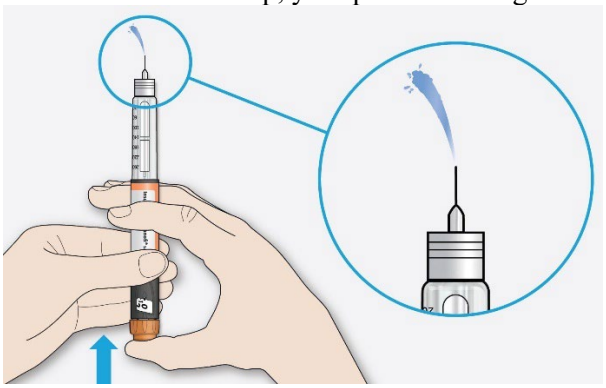
- Always do a safety test before each injection – this is to:
  - check your pen and the needle are working properly.
  - make sure that you get the correct insulin dose.

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



3B 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.

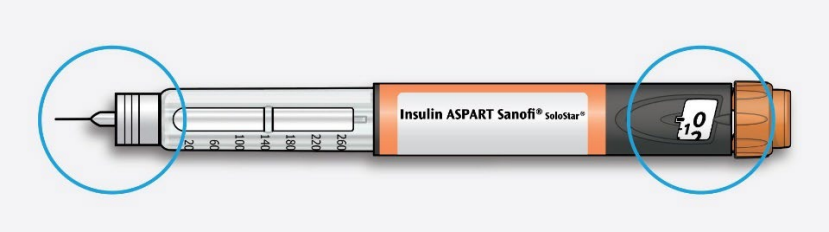
If you see air bubbles

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

STEP 4: Select the dose

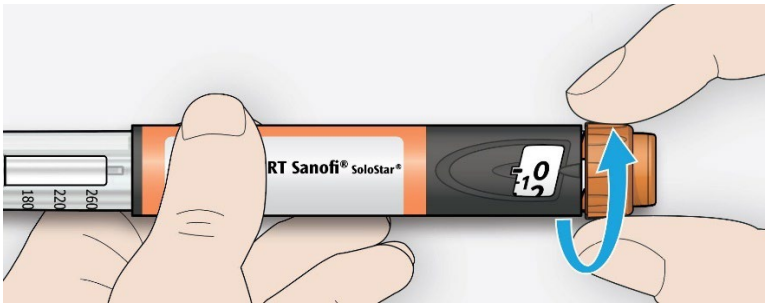
- Never select a dose or press the injection button without a needle attached. This may damage your pen.

4A Make sure a needle is attached and the dose is set to '0'.



4B 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, use a new pen or inject the remaining units and use a new pen to complete your dose.



How to read the dose window

Even numbers are shown in line with the dose pointer:



20 units selected

Odd numbers are shown as a line between even numbers:



21 units selected

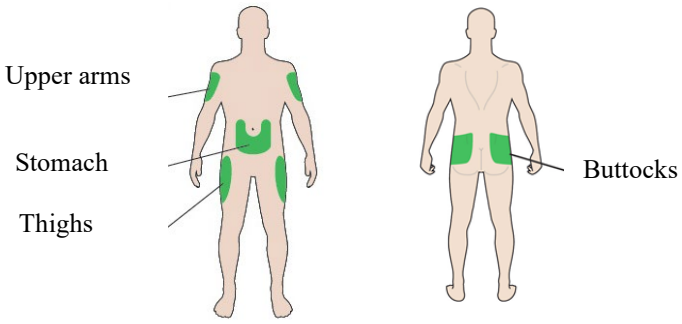
Units of insulin in your pen

- Your pen contains a total of 300 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

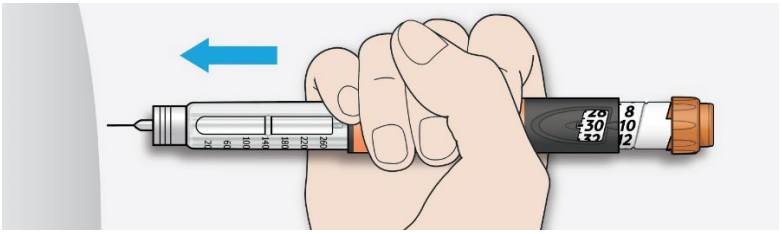
- If you find it hard to press the injection button in, do not force it as this may break your pen. See the i section below for help.

5A Choose a place to inject as shown in the picture



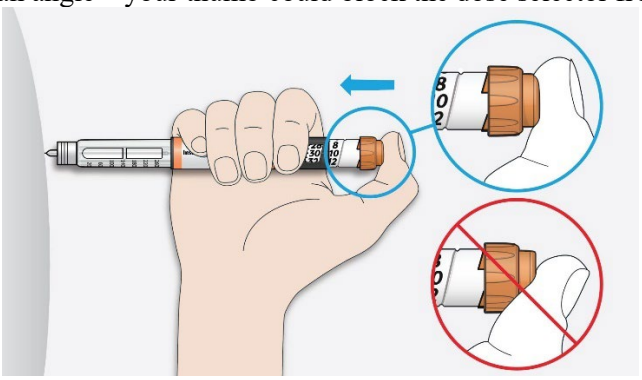
5B Push the needle into your skin as shown by your doctor, pharmacist or nurse.

- Do not touch the injection button yet.



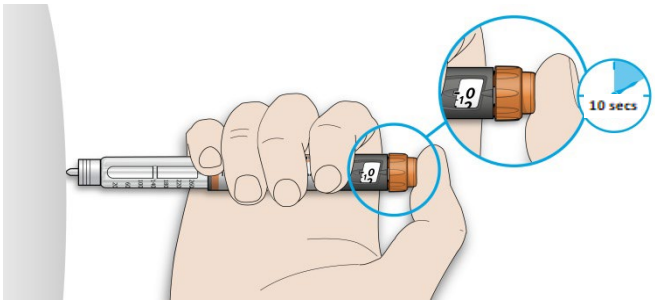
5C Place your thumb on the injection button. Then press all the way in and hold.

- Do not press at an angle – your thumb could block the dose selector from turning.



5D Keep the injection button held in and when you see "0" in the dose window, slowly count to 10.

- This will make sure you get your full dose.



5E After holding and slowly counting to 10, release the injection button. Then remove the needle from your skin.

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.

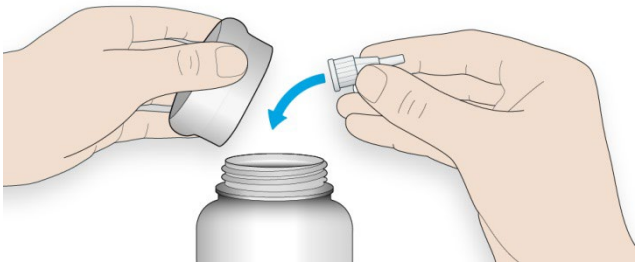
STEP 6: Remove the needle

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

6A Put the outer needle cap back on the needle, and use it to unscrew the needle from the pen.

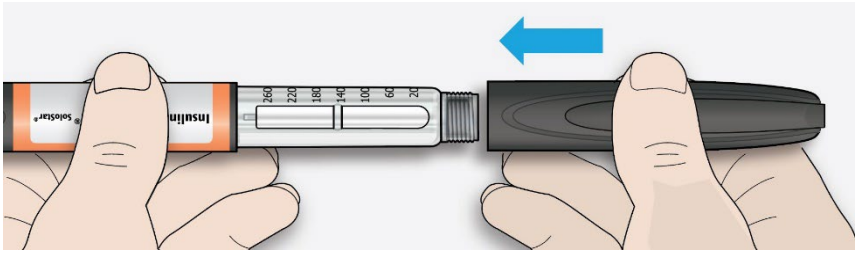
- To reduce the risk of accidental needle injury, never replace the inner needle cap.
- If your injection is given by another person, or if you are giving an injection to another person, special caution must be taken by this person when removing and disposing of the needle.
- Follow recommended safety 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.

6B Throw away the used needle in a puncture resistant container, or as told by your pharmacist or local authority.



6C Put the pen cap back on.

- Do not put the pen back in the fridge.



How to store and care for you pen

- You can clean the outside of your pen by wiping it with a damp cloth (water only). Do not soak, wash or lubricate your pen – this may damage it.
- Remove the needle and throw away your used pen as told by your pharmacist or local authority.
- For further information on the storage and use of your pen please refer to sections 2 and 5 of the package leaflet.