ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Truvelog Mix 30 100 units/mL suspension for injection in cartridge
Truvelog Mix 30 100 units/mL suspension for injection in pre-filled pen

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One mL suspension contains 100 units soluble insulin aspart*/protamine-crystallised insulin aspart* in the ratio 30/70 (equivalent to 3.5 mg).

Truvelog Mix 30 100 units/mL suspension for injection in cartridge

Each cartridge contains 3 mL equivalent to 300 units.

Truvelog Mix 30 100 units/mL suspension for injection in pre-filled pen

Each pre-filled pen contains 3 mL equivalent to 300 units.

Each pre-filled pen injection 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

Truvelog Mix 30 100 units/mL suspension for injection in cartridge

Suspension for injection.

Truvelog Mix 30 100 units/mL suspension for injection in pre-filled pen

Suspension for injection in pre-filled pen (SoloStar).

The suspension is cloudy and white.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Truvelog Mix 30 is indicated for treatment of diabetes mellitus in adults, adolescents and children aged 10 years 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.

Truvelog Mix 30 dosing is individual and determined in accordance with the needs of the patient. Blood glucose monitoring and insulin dose adjustments are recommended to achieve optimal glycaemic control.

In patients with type 2 diabetes, Truvelog Mix 30 can be given as monotherapy. Truvelog Mix 30 can also be given in combination with oral antidiabetic medicinal products and/or GLP-1 receptor agonists. For patients with type 2 diabetes, the recommended starting dose of Truvelog Mix 30 is 6 units at breakfast and 6 units at dinner (evening meal). Truvelog Mix 30 can also be initiated once daily with 12 units at dinner (evening meal). When using Truvelog Mix 30 once daily, it is generally recommended to move to twice daily when reaching 30 units by splitting the dose into equal breakfast and dinner doses. If twice daily dosing with Truvelog Mix 30 results in recurrent daytime hypoglycaemic episodes, the morning dose can be split into morning and lunchtime doses (thrice daily dosing).

The following titration guideline is recommended for dose adjustments:

Pre-meal blood glucose level		Truvelog Mix 30 dose adjustment
<4.4 mmol/L	<80 mg/dL	-2 units
4.4–6.1 mmol/L	80–110 mg/dL	0
6.2–7.8 mmol/L	111–140 mg/dL	+2 units
7.9–10 mmol/L	141–180 mg/dL	+4 units
>10 mmol/L	>180 mg/dL	+6 units

The lowest of the three previous days' pre-meal blood glucose levels should be used. The dose should not be increased if hypoglycaemia occurred within these days. Dose adjustments can be made once a week until target HbA_{1c} is reached. Pre-meal blood glucose levels should be used to evaluate the adequacy of the preceding dose.

In patients with type 2 diabetes, a dose reduction of 20% is recommended for patients with an HbA_{1c} less than 8% when a GLP-1 receptor agonist is added to Truvelog Mix 30, to minimise the risk of hypoglycaemia. For patients with an HbA_{1c} higher than 8% a dose reduction should be considered. Subsequently, dose should be adjusted individually.

In patients with type 1 diabetes, the individual insulin requirement is usually between 0.5 and 1 unit/kg/day. Truvelog Mix 30 may fully or partially meet this requirement.

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 a patient from a treatment regimen with another premix insulin therapy with the same ratio as Truvelog Mix 30, the switch of the insulin should be done on a unit to unit (1:1) basis (no conversion needed) under strict medical supervision with titration according to individual needs (see the titration guideline in the table above).

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

Special populations
Elderly (≥65 years old)

Truvelog Mix 30 can be used in elderly patients; however there is limited experience with the use of Truvelog Mix 30 in combination with oral antidiabetic medicinal products in patients older than 75 years.

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

Truvelog Mix 30 can be used in adolescents and children aged 10 years and above when premixed insulin is preferred. There is limited clinical experience with Truvelog Mix 30 in children aged 6-9 years (see section 5.1).

No data are available for Truvelog Mix 30 in children below 6 years of age.

Method of administration

Truvelog Mix 30 is a biphasic suspension of the insulin analogue, insulin aspart. The suspension contains rapid-acting and intermediate-acting insulin aspart in the ratio 30/70.

Truvelog Mix 30 is for subcutaneous administration **only**.

Before every injection with Truvelog Mix 30,the insulin must be mixed by rolling and moving the pen until the liquid appears uniformly white and cloudy.

Truvelog Mix 30 is administered subcutaneously by injection in the thigh or in the abdominal wall. If convenient, the gluteal or deltoid region may be used. Injection sites should always be rotated within the same region in order to reduce the risk of lipodystrophy and cutaneous amyloidosis (see sections 4.4 and 4.8). The influence of different injection sites on the absorption of Truvelog Mix 30 has not been investigated. The duration of action will vary according to the dose, injection site, blood flow, temperature and level of physical activity.

Truvelog Mix 30 has a faster onset of action than biphasic human insulin and should generally be given immediately before a meal. When necessary, Truvelog Mix 30 can be given soon after a meal.

Truvelog Mix 30 must not be administered intravenously, as it may result in severe hypoglycaemia. Intramuscular administration should be avoided. Truvelog Mix 30 is not to be used in insulin infusion pumps.

Truvelog Mix 30 100 units/mL suspension for injection in cartridge
Truvelog Mix 30 in cartridges is only suitable for subcutaneous injections from a reusable pen (see section 4.4). Truvelog Mix 30 in cartridges is designated to be used in the following pens (see section 6.6):

- AllStar and AllStar PRO which deliver 1-80 units of insulin aspart per injection in 1 unit dose increments.

Truvelog Mix 30 100 units/mL suspension for injection in pre-filled pen

Truvelog Mix 30 in pre-filled pen is only suitable for subcutaneous injections. If administration by syringe is necessary, another insulin medicinal product offering a vial should be used (see section 4.4). Truvelog Mix 30 in pre-filled pen delivers 1-80 units of insulin aspart per injection 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 product should be clearly recorded.

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.

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, Truvelog Mix 30 must not be injected. After stabilisation of the patient's blood glucose, adjustment of the dose should be considered (see sections 4.2, 4.8 and 4.9).

Compared with biphasic human insulin, Truvelog Mix 30 may have a more pronounced glucose lowering effect up to 6 hours after injection. This may have to be compensated for in the individual patient through adjustment of insulin dose and/or food intake.

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.

Tighter control of glucose levels can increase the potential for hypoglycaemic episodes and therefore require special attention during dose intensification as outlined in section 4.2.

Since Truvelog Mix 30 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 Truvelog Mix 30 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 Truvelog Mix 30.

Skin and subcutaneous tissue disorders

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 from an affected to an unaffected area, and dose adjustment of antidiabetic medicinal products may be considered.

Combination of Truvelog Mix 30 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 Truvelog Mix 30 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 Truvelog Mix 30 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.

Excipients

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, GLP-1 receptor agonists, monoamine oxidase inhibitors (MAOI), beta-blockers, angiotensin converting enzyme (ACE) inhibitors, salicylates, anabolic steroids and sulfonamides.

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

There is limited clinical experience with Truvelog Mix 30 in pregnancy.

Animal reproduction studies have not revealed any differences between insulin aspart and human insulin regarding embryotoxicity or teratogenicity.

In general, intensified blood glucose control and monitoring of pregnant women with 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 trimesters. After delivery, insulin requirements return rapidly to pre-pregnancy levels.

Breast-feeding

There are no restrictions on treatment with Truvelog Mix 30 during breast-feeding. Insulin treatment of the breast-feeding mother presents no risk to the baby. However, the Truvelog Mix 30 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 or using a machine. 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 Truvelog Mix 30 are mainly due to the pharmacological effect of insulin aspart.

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		Lipodystrophy*			Cutaneous amyloidosis*†

tissue disorders					
General disorders and administration site conditions		Injection site reactions, oedema			

*see Description of selected adverse reactions
† ADR from post-marketing sources.

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 concentrating, 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, 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, the frequency, type and severity of adverse reactions observed in 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, intermediate- or long-acting combined with fast-acting, ATC code: A10AD05

Truvelog Mix 30 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

Truvelog Mix 30 is a biphasic suspension of 30% soluble insulin aspart (rapid-acting human insulin analogue) and 70% protamine-crystallised insulin aspart (intermediate-acting human insulin analogue).

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.

Truvelog Mix 30 is a biphasic insulin, which contains 30% soluble insulin aspart. This has a rapid onset of action, thus allowing it to be given closer to a meal (within zero to 10 minutes of the meal) when compared to soluble human insulin. The crystalline phase (70%) consists of protamine-crystallised insulin aspart, which has an activity profile similar to that of human NPH insulin.

When Truvelog Mix 30 is injected subcutaneously, the onset of action will occur within 10 to 20 minutes of injection. The maximum effect is exerted between 1 and 4 hours after injection. The duration of action is up to 24 hours (Figure 1).

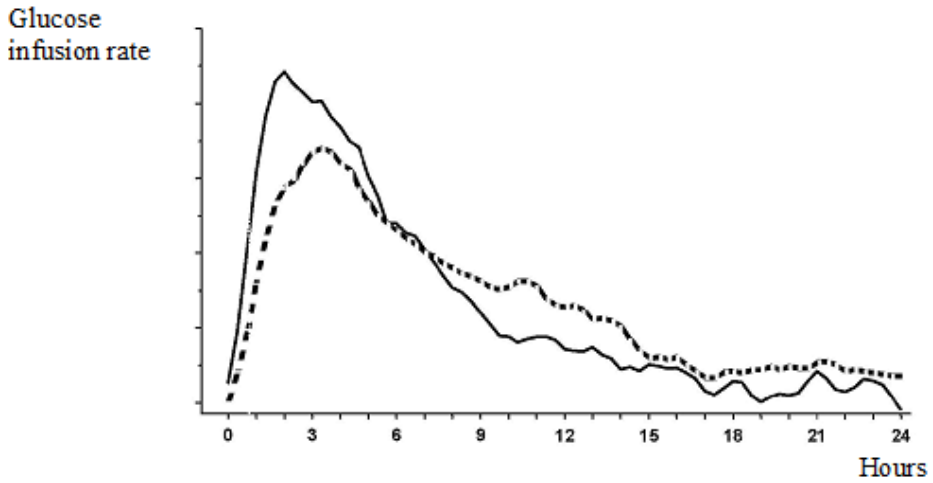

Figure 1: Activity profile of insulin aspart Mix 30 (−) and biphasic human insulin 30 (---) in healthy subjects.

Clinical efficacy and safety

In a 3-month trial in patients with type 1 and type 2 diabetes, insulin aspart Mix 30 showed equal control of glycosylated haemoglobin compared to treatment with biphasic human insulin 30. Insulin aspart is equipotent to human insulin on a molar basis. Compared to biphasic human insulin 30, administration of insulin aspart Mix 30 before breakfast and dinner resulted in lower postprandial blood glucose after both meals (breakfast and dinner).

A meta-analysis including nine trials in patients with type 1 and type 2 diabetes showed that fasting blood glucose was higher in patients treated with insulin aspart Mix 30, than in patients treated with biphasic human insulin 30.

In one trial, 341 patients with type 2 diabetes were randomised to treatment with insulin aspart Mix 30 either alone or in combination with metformin, or to metformin together with sulfonylurea. The primary efficacy variable - HbA_{1c} after 16 weeks of treatment - did not differ between patients with insulin aspart Mix 30 combined with metformin and patients with metformin plus sulfonylurea. In this trial, 57% of the patients had baseline HbA_{1c} above 9%; in these patients, treatment with insulin aspart Mix 30 in combination with metformin resulted in significantly lower HbA_{1c} than metformin in combination with sulfonylurea.

In one trial, patients with type 2 diabetes, insufficiently controlled on oral hypoglycaemic agents alone, were randomised to treatment with twice daily insulin aspart Mix 30 (117 patients) or once daily insulin glargine (116 patients). After 28 weeks of treatment following the dosing guideline outlined in section 4.2, the mean reduction in HbA_{1c} was 2.8% with insulin aspart Mix 30 (mean at baseline = 9.7%). With insulin aspart Mix 30, 66% and 42% of the patients reached HbA_{1c} levels below 7% and 6.5%, respectively, and mean FPG was reduced by about 7 mmol/L (from 14 mmol/L at baseline to 7.1 mmol/L).

In patients with type 2 diabetes, a meta-analysis showed a reduced risk of overall nocturnal hypoglycaemic episodes and major hypoglycaemia with insulin aspart Mix 30 compared to biphasic human insulin 30. The risk of overall daytime hypoglycaemic episodes was increased in patients treated with insulin aspart Mix 30.

Paediatric population

A 16-week clinical trial comparing postprandial glycaemic control of meal-related insulin aspart Mix 30 with meal-related human insulin/biphasic human insulin 30 and bedtime NPH insulin was performed in 167 patients aged 10 to 18 years. Mean HbA_{1c} remained similar to baseline throughout

the trial in both treatment groups, and there was no difference in hypoglycaemia rate with insulin aspart Mix 30 or biphasic human insulin 30.

In a smaller (54 patients) and younger (age range 6 to 12 years) population, treated in a double-blind, cross-over trial (12 weeks on each treatment), the rate of hypoglycaemic episodes and the postprandial glucose increase were significantly lower with insulin aspart Mix 30 compared to biphasic human insulin 30. Final HbA_{1c} was significantly lower in the biphasic human insulin 30 treated group compared with insulin aspart Mix 30.

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. The insulin aspart in the soluble phase of Truvelog Mix 30 comprises 30% of the total insulin; this is absorbed more rapidly from the subcutaneous layer than the soluble insulin component of biphasic human insulin. The remaining 70% is in crystalline form as protamine-crystallised insulin aspart; this has a prolonged absorption profile similar to human NPH insulin.

The maximum serum insulin concentration is, on average, 50% higher with insulin aspart Mix 30 than with biphasic human insulin 30. The time to maximum concentration is, on average, half of that for biphasic human insulin 30. In healthy volunteers, a mean maximum serum concentration of 140 ± 32 pmol/L was reached about 60 minutes after a subcutaneous dose of 0.20 unit/kg body weight. The mean half-life ($t_{½}$) of insulin aspart Mix 30, reflecting the absorption rate of the protamine bound fraction, was about 8-9 hours. Serum insulin levels returned to baseline 15-18 hours after a subcutaneous dose. In type 2 diabetic patients, the maximum concentration was reached about 95 minutes after dosing, and concentrations well above zero for not less than 14 hours post-dosing were measured.

Special populations

The pharmacokinetics of insulin aspart Mix 30 have not been investigated in elderly patients or in patients with renal or hepatic impairment.

Paediatric population
The pharmacokinetics of insulin aspart Mix 30 have not been investigated in children or adolescents. However, the pharmacokinetic and pharmacodynamic properties of soluble insulin aspart have been 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

Glycerol

Phenol
Metacresol
Zinc chloride
Disodium hydrogen phosphate heptahydrate
Sodium chloride
Protamine sulfate
Hydrochloric acid (for pH adjustment)
Sodium hydroxide (for pH adjustment)
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

Before opening for first use

2 years

After first use

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

6.4 Special precautions for storage

Truvelog Mix 30 100 units/mL suspension for injection in cartridge

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

Truvelog Mix 30 100 units/mL suspension for injection in pre-filled pen

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.

For storage conditions after first use of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Truvelog Mix 30 100 units/mL suspension 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 suspension. The cartridge contains steel balls to facilitate resuspension.
Pack sizes: 5 or 10 cartridges. Not all pack sizes may be marketed.

Truvelog Mix 30 100 units/mL suspension 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). The cartridge contains steel balls to facilitate resuspension.
Each pre-filled pen contains 3 mL of suspension.

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

After removing Truvelog Mix 30 from the refrigerator, it is recommended to allow Truvelog Mix 30 to reach room temperature for 1 to 2 hours before resuspending the insulin as instructed for first time use. This medicinal product must not be used if the resuspended liquid is not uniformly white and cloudy. The necessity of resuspending the Truvelog Mix 30 suspension immediately before use is to be stressed to the patient. Truvelog Mix 30 which has been frozen must not be used.
Always use a new needle for each injection.

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

Truvelog Mix 30 100 units/mL suspension 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.

Truvelog Mix 30 in cartridges are to be used with AllStar or AllStar PRO pens as recommended (see section 4.2 and 4.4).

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

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

The cartridge must not be refilled.

Truvelog Mix 30 100 units/mL suspension 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.
Needles are not included in the pack.

7. MARKETING AUTHORISATION HOLDER

sanofi-aventis groupe
54, rue La Boétie
F - 75008 Paris
France

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/22/1639/001
EU/1/22/1639/002
EU/1/22/1639/003
EU/1/22/1639/004
EU/1/22/1639/005

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation:

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

Sanofi-Aventis Private Co. Ltd.,
Budapest Logistics and Distribution Platform
Bdg. DC5, Campona utca 1.,
Budapest, 1225, Hungary

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

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (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

LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (CARTRIDGE)

1. NAME OF THE MEDICINAL PRODUCT

Truvelog Mix 30 100 units/mL suspension for injection in cartridge
30% soluble insulin aspart and 70% insulin aspart crystallised with protamine

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One mL suspension contains 100 units soluble insulin aspart/protamine-crystallised insulin aspart in the ratio 30/70 (equivalent to 3.5 mg).
Each cartridge contains 3 mL equivalent to 300 units.

3. LIST OF EXCIPIENTS

Excipients: glycerol, phenol, metacresol, zinc chloride, disodium hydrogen phosphate heptahydrate, sodium chloride, protamine sulfate, hydrochloric acid/sodium hydroxide (for pH adjustment), water for injections. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection

5 x 3 mL cartridges
10 x 3 mL cartridges

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Use the cartridges only with the pens: AllStar, AllStar PRO.
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

Resuspend according to instructions.
Only use resuspension if it appears uniformly white and cloudy.
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-aventis groupe
54, rue La Boétie
F - 75008 Paris
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/22/1639/004 5 cartridges
EU/1/22/1639/005 10 cartridges

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Truvelog Mix 30

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

Truvelog Mix 30 100 units/mL suspension for injection
30% soluble insulin aspart and 70% insulin aspart crystallised with protamine
subcutaneous use

2. METHOD OF ADMINISTRATION

Resuspend according to instructions.

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3 mL

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (PRE-FILLED PEN. SoloStar)

1. NAME OF THE MEDICINAL PRODUCT

Truvelog Mix 30 100 units/mL suspension for injection in pre-filled pen
30% soluble insulin aspart and 70% insulin aspart crystallised with protamine

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One mL suspension contains 100 units soluble insulin aspart/protamine-crystallised insulin aspart in the ratio 30/70 (equivalent to 3.5 mg).
Each pen contains 3 mL equivalent to 300 units.
Each pen delivers 1-80 units in steps of 1 unit.

3. LIST OF EXCIPIENTS

Excipients: glycerol, phenol, metacresol, zinc chloride, disodium hydrogen phosphate heptahydrate, sodium chloride, protamine sulfate, hydrochloric acid/sodium hydroxide (for pH adjustment), water for injections. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection in pre-filled pen SoloStar

1 pre-filled pen of 3 mL
5 pre-filled pens of 3 mL
10 pre-filled pens of 3 mL

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Open here
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

Resuspend according to instructions.
Only use resuspension if it appears uniformly white and cloudy.
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-aventis groupe
54, rue La Boétie
F - 75008 Paris
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/22/1639/001 1 pre-filled pen
EU/1/22/1639/002 5 pre-filled pens
EU/1/22/1639/003 10 pre-filled pens

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Truvelog Mix 30 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

Truvelog Mix 30 100 units/mL suspension for injection
30% soluble insulin aspart and 70% insulin aspart crystallised with protamine
subcutaneous use

2. METHOD OF ADMINISTRATION

Resuspend according to instructions

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

Truvelog Mix 30 100 units/mL suspension for injection in cartridge
30% soluble insulin aspart and 70% insulin aspart crystallised with protamine

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

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 Truvelog Mix 30 is and what it is used for
2. What you need to know before you use Truvelog Mix 30
3. How to use Truvelog Mix 30
4. Possible side effects
5. How to store Truvelog Mix 30
6. Contents of the pack and other information

1. What Truvelog Mix 30 is and what it is used for

Truvelog Mix 30 is a modern insulin (insulin analogue) with both a rapid-acting and an intermediate-acting effect, in the ratio 30/70. Modern insulin medicines are improved versions of human insulin.

Truvelog Mix 30 is used to reduce the high blood sugar level in adults, adolescents and children aged 10 years 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.

Truvelog Mix 30 will start to lower your blood sugar 10–20 minutes after you inject it, the maximum effect occurs between 1 and 4 hours after the injection, and the effect lasts for up to 24 hours.

In treatment of type 2 diabetes mellitus, Truvelog Mix 30 may be used in combination with tablets for diabetes and/or with injectable antidiabetic medicines.

2. What you need to know before you use Truvelog Mix 30

Do not use Truvelog Mix 30
- If you are allergic to insulin aspart or any of the other ingredients in this medicine (listed in section 6).
- If you suspect hypoglycaemia (low blood sugar) is starting, see a) Summary of serious and very common side effects in section 4.
- In insulin infusion pumps.
- If the cartridge or the device containing the cartridge is dropped, damaged or crushed.
- If it has not been stored correctly or if it has been frozen, see section 5, How to store Truvelog Mix 30.
- If the resuspended insulin does not appear uniformly cloudy and white.
- If after resuspension, clumps of material are present or if solid white particles stick to the bottom

or the wall of the cartridge.
If any of these apply, do not use Truvelog Mix 30. Talk to your doctor, nurse or pharmacist for advice.

Before using Truvelog Mix 30
- 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. If you suspect that 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 cartridges of Truvelog Mix 30 must not be shared.
- Truvelog Mix 30 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 ("Truvelog Mix 30") 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.

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 hereof.

Skin changes at the injection site
The injection site should be rotated to help prevent changes to the fatty tissue under the skin, such as skin thickening, skin shrinking or lumps under the skin. The insulin may not work very well if you inject into a lumpy, shrunken or thickened area (see section 3, How to use Truvelog Mix 30). Tell your doctor if you notice any skin changes at the injection site. Tell your doctor if you are currently injecting into these affected areas 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 medicines dose.

Children and adolescents
- Truvelog Mix 30 can be used in adolescents and children aged 10 years and above.
- There is limited experience with Truvelog Mix 30 in children aged 6–9 years.
- No data are available for Truvelog Mix 30 in children below 6 years of age.

Other medicines and Truvelog Mix 30
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)
- Sulfonamides (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], salbutamol or 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.

Truvelog Mix 30 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 taking this medicine. There is limited clinical experience with insulin aspart in 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 Truvelog Mix 30 during breast-feeding.

Ask your doctor, nurse or pharmacist for advice before taking any 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, it might affect your concentration and ability to react and therefore also your ability to drive or use a machine. Bear in mind that you could endanger yourself or others.

Truvelog Mix 30 contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially "sodium-free".

3. How to use Truvelog Mix 30

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.

Truvelog Mix 30 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, Truvelog Mix 30 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.

When Truvelog Mix 30 is used in combination with tablets for diabetes and/or with injectable antidiabetic medicines your dose may have to be adjusted by your doctor.

Use in children and adolescents
Truvelog Mix 30 can be used in adolescents and children aged 10 years and above when premixed insulin is preferred. Limited clinical data exists for children aged 6–9 years. No data are available for Truvelog Mix 30 in children below 6 years of age.

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 and where to inject
Truvelog Mix 30 is for injection under the skin (subcutaneously). Never inject your insulin directly into a vein (intravenously) or muscle (intramuscularly). Truvelog Mix 30 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); your buttocks; the front of your thighs or upper arms. The insulin will work more quickly if you inject around the waist. You should always measure your blood sugar regularly.

- Do not refill the cartridge.
- Truvelog Mix 30 in cartridges are to be used only with the following pens:
  - AllStar and AllStar PRO which deliver doses in steps of 1 unit.
- If you are treated with Truvelog Mix 30 in cartridge using AllStar or AllStar PRO and another insulin in cartridge using alsoAllStar or AllStar PRO, you should use two insulin delivery systems, one for each type of insulin.
- Always carry a spare cartridge in case the one in use is lost or damaged.

Resuspension of Truvelog Mix 30
Always check if there is enough insulin left in the cartridge to allow even resuspension. If there is not enough insulin left, use a new one. See your pen manual for further instructions.

Every time you use a new cartridge of Truvelog Mix 30 (before you put the cartridge into the insulin delivery system)
- Keep the cartridge at room temperature for 1 or 2 hours before inserting it into the pen.
- Mixing is best done by gently tilting the cartridge or pen (with the cartridge in it) back and forth at least 10 times.
- To assist in mixing, three tiny metal balls are present in the cartridge.

- After mixing, the suspension must have a uniform cloudy and white appearance. It must not be used if it remains clear or if, for example, clumps, flakes, particles or anything similar are in the suspension or on the sides or bottom of the cartridge. A new cartridge with a uniform suspension on mixing must then be used.
- Complete the other stages of injection without delay.
- For every following injection, you must mix the insulin well again immediately before each injection.

How to inject Truvelog Mix 30
- Inject the insulin under your 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 push-button fully depressed until the needle has been withdrawn from the skin. This will ensure correct delivery and limit possible flow of blood into the needle or insulin reservoir.
- After each injection, be sure to remove and discard the needle and store Truvelog Mix 30 without the needle attached. Otherwise the liquid may leak out, which can cause inaccurate dosing.

Special care before injection
Before injection remove any air bubbles (see instructions for using the pen). Make sure that neither alcohol nor other disinfectants or other substances contaminate the insulin.
- Do not re-fill and re-use empty cartridges.
- Do not add any other insulin to the cartridge.
- Do not mix insulin with any other medicines.

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

If you use more insulin than you should
If you use too much insulin, your blood sugar gets too low (hypoglycaemia). See a) 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 c) 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 c) 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.

a) 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 Truvelog Mix 30 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 given 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 the symptoms of low blood sugar have disappeared or when your blood sugar level is stabilised, continue insulin treatment as usual.
- If you have such low blood sugar that it makes you pass out, if you have had the need for an injection of glucagon, or if you have experienced many incidents of low blood sugar, talk to 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 (becoming 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 because you may choke.

Serious allergic reactions to Truvelog Mix 30 or one of its other ingredients (called a systemic allergic reaction) is a very rare side effect, but it can potentially be life-threatening. It may affect less than 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.

Skin changes at the injection site: if you inject insulin at the same place, the fatty tissue may shrink (lipoatrophy) or thicken (lipohypertrophy) (may affect less than 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, shrunken or thickened area. Change the injection site with each injection to help prevent these skin changes.

b) List of other side effects
Uncommon side effects (may affect less than 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 taking your insulin. If they do not disappear, see your doctor.

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, contact 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 less than 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, pharmacist or nurse. 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.

c) 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 Truvelog Mix 30

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 after EXP. The expiry date refers to the last day of that month.

Before the first use, store your Truvelog Mix 30 in a refrigerator (2°C – 8°C). Do not freeze. Keep the cartridge in the outer carton in order to protect from light. It is recommended to resuspend the insulin as instructed every time you use a new cartridge of Truvelog Mix 30. See Resuspension of Truvelog Mix 30 in section 3.

During use, 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 throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Truvelog Mix 30 contains
- The active substance is insulin aspart. Truvelog Mix 30 is a mixture consisting of 30% soluble insulin aspart and 70% insulin aspart crystallised with protamine. 1 mL contains 100 units of insulin aspart. Each cartridge contains 300 units of insulin aspart in 3 mL suspension for injection.
- The other ingredients are glycerol, phenol, metacresol, zinc chloride, disodium hydrogen phosphate heptahydrate, sodium chloride, protamine sulfate, hydrochloric acid, sodium hydroxide and water for injections (see section 2 “Truvelog Mix 30 contains sodium”).

What Truvelog Mix 30 looks like and contents of the pack
Truvelog Mix 30 is presented as a suspension for injection. The cartridge contains metal balls to facilitate resuspension. After resuspension, the liquid should appear uniformly cloudy and white. Do not use the insulin, if it does not look uniformly cloudy and white after resuspension.

Truvelog Mix 30 cartridges come in a pack of 5 or 10 cartridges of 3 mL.
Not all pack sizes may be marketed.

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Manufacturer
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This leaflet was last revised in

Other sources of information
Detailed information on this medicine is available on the website of the European Medicines Agency http://www.ema.europa.eu.

Package leaflet: information for the user

Truvelog Mix 30 100 units/mL suspension for injection in pre-filled pen
30% soluble insulin aspart and 70% insulin aspart crystallised with protamine

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

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 Truvelog Mix 30 is and what it is used for
2. What you need to know before you use Truvelog Mix 30
3. How to use Truvelog Mix 30
4. Possible side effects
5. How to store Truvelog Mix 30
6. Contents of the pack and other information

1. What Truvelog Mix 30 is and what it is used for

Truvelog Mix 30 is a modern insulin (insulin analogue) with both a rapid-acting and an intermediate-acting effect, in the ratio 30/70. Modern insulin medicines are improved versions of human insulin.

Truvelog Mix 30 is used to reduce the high blood sugar level in adults, adolescents and children aged 10 years 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.

Truvelog Mix 30 will start to lower your blood sugar 10–20 minutes after you inject it, the maximum effect occurs between 1 and 4 hours after the injection, and the effect lasts for up to 24 hours.
In treatment of type 2 diabetes mellitus, Truvelog Mix 30 may be used in combination with tablets for diabetes and/or with injectable antidiabetic medicines.

2. What you need to know before you use Truvelog Mix 30

Do not use Truvelog Mix 30
- If you are allergic to insulin aspart or any of the other ingredients in this medicine (listed in section 6).
- If you suspect hypoglycaemia (low blood sugar) is starting, see a) Summary of serious and very common side effects in section 4.
- In insulin infusion pumps.
- If the pre-filled pen is dropped, damaged or crushed.
- If it has not been stored correctly or if it has been frozen, see section 5, How to store Truvelog Mix 30.
- If the resuspended insulin does not appear uniformly cloudy and white.
- If after resuspension, clumps of material are present or if solid white particles stick to the bottom or the wall of the cartridge.

If any of these apply, do not use Truvelog Mix 30. Talk to your doctor, nurse or pharmacist for advice.

Before using Truvelog Mix 30
- 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.
- Truvelog Mix 30 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 ("Truvelog Mix 30") 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.

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 hereof.

Skin changes at the injection site
The injection site should be rotated to help prevent changes to the fatty tissue under the skin, such as skin thickening, skin shrinking or lumps under the skin. The insulin may not work very well if you inject into a lumpy, shrunken or thickened area (see section 3, How to use Truvelog Mix 30). Tell your doctor if you notice any skin changes at the injection site. Tell your doctor if you are currently injecting into these affected areas 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 medicines dose.

Children and adolescents
- Truvelog Mix 30 can be used in adolescents and children aged 10 years and above.
- There is limited experience with Truvelog Mix 30 in children aged 6–9 years.
- No data are available for Truvelog Mix 30 in children below 6 years of age.

Other medicines and Truvelog Mix 30
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)
- Sulfonamides (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], salbutamol or 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.

Truvelog Mix 30 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 taking this medicine. There is limited clinical experience with insulin aspart in 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 Truvelog Mix 30 during breast-feeding.

Ask your doctor, nurse or pharmacist for advice before taking any 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, it might affect your concentration and ability to react and therefore also your ability to drive or use a machine. Bear in mind that you could endanger yourself or others.

Truvelog Mix 30 contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially "sodium-free".

3. How to use Truvelog Mix 30

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.

Truvelog Mix 30 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, Truvelog Mix 30 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.

When Truvelog Mix 30 is used in combination with tablets for diabetes and/or with injectable antidiabetic medicines your dose may have to be adjusted by your doctor.

Use in children and adolescents
Truvelog Mix 30 can be used in adolescents and children aged 10 years and above when premixed insulin is preferred. Limited clinical data exists for children aged 6–9 years. No data are available for Truvelog Mix 30 in children below 6 years of age.

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 and where to inject
Truvelog Mix 30 is for injection under the skin (subcutaneously). Never inject your insulin directly into a vein (intravenously) or muscle (intramuscularly). Truvelog Mix 30 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); your buttocks; the front of your thighs or upper arms. The insulin will work more quickly if you inject around the waist. You should always measure your blood sugar regularly.

How to handle Truvelog Mix 30 pre-filled pen (SoloStar)
Truvelog Mix 30 is a colour-coded, disposable pre-filled pen (SoloStar) containing a mixture of rapid-acting and intermediate-acting insulin aspart in the ratio 30/70.

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 a) 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 c) 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 c) 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.

a) 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 Truvelog Mix 30 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 given 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 the symptoms of low blood sugar have disappeared or when your blood sugar level is stabilised, continue insulin treatment as usual.
- If you have such low blood sugar that it makes you pass out, if you have had the need for an injection of glucagon, or if you have experienced many incidents of low blood sugar, talk to 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 (becoming 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 because you may choke.

Serious allergic reactions to Truvelog Mix 30 or one of its other ingredients (called a systemic allergic reaction) is a very rare side effect, but it can potentially be life-threatening. It may affect less than 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.

Skin changes at the injection site: If you inject insulin at the same place, the fatty tissue may shrink (lipoatrophy) or thicken (lipohypertrophy) (may affect less than 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, shrunken or thickened area. Change the injection site with each injection to help prevent these skin changes.

b) List of other side effects

Uncommon side effects (may affect less than 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 taking your insulin. If they do not disappear, see your doctor.

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, contact 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 less than 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, pharmacist or nurse. 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.

c) 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 Truvelog Mix 30

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 after EXP. The expiry date refers to the last day of that month.

Before the first use, store your Truvelog Mix 30 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.

During use, keep your Truvelog Mix 30 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 throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Truvelog Mix 30 contains
- The active substance is insulin aspart. Truvelog Mix 30 is a mixture consisting of 30% soluble insulin aspart and 70% insulin aspart crystallised with protamine. 1 mL contains 100 units of insulin aspart. Each pre-filled pen contains 300 units of insulin aspart in 3 mL suspension for injection.
- The other ingredients are glycerol, phenol, metacresol, zinc chloride, disodium hydrogen phosphate heptahydrate, sodium chloride, protamine sulfate, hydrochloric acid, sodium hydroxide and water for injections (See section 2 “Truvelog Mix 30 contains sodium”).

What Truvelog Mix 30 looks like and contents of the pack
Truvelog Mix 30 is presented as a suspension for injection in pre-filled pen. The pre-filled pen contains metal balls to facilitate resuspension. After resuspension, the liquid should appear uniformly cloudy and white. Do not use the insulin, if it does not look uniformly cloudy and white after resuspension.

Pack sizes of 1, 5 or 10 pre-filled pens of 3 mL. Needles are not included in the pack. Not all pack sizes may be marketed.

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This leaflet was last revised in

Other sources of information
Detailed information on this medicine is available on the website of the European Medicines Agency http://www.ema.europa.eu.

Truvelog Mix 30 suspension 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 get 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.

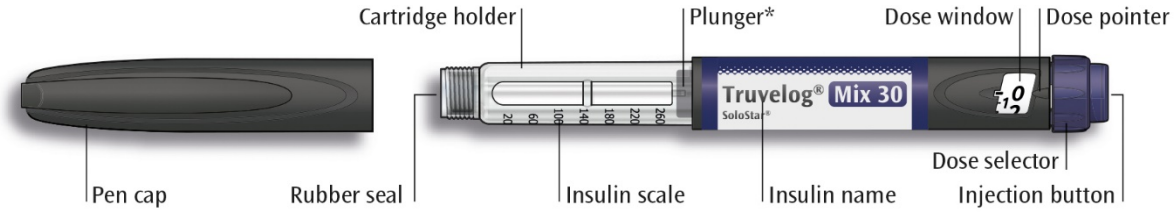
Need help?

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

Extra items you will need:

- a new sterile needle (not included with the pen) (see **Step 2**).
- an alcohol swab.
- 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.

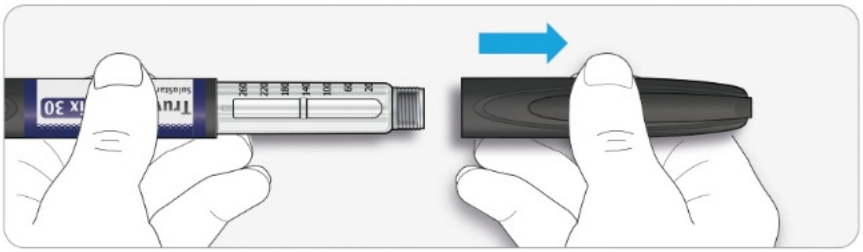
STEP 1: Check and mix your pen

- Take a new pen out of the fridge at least 1 hour before you inject. This makes it easier to mix. Cold insulin is more painful to inject.
- Before your first injection with the Truvelog Mix 30 (SoloStar) you must mix the insulin.

1A Check the name and expiry date on the label of your pen

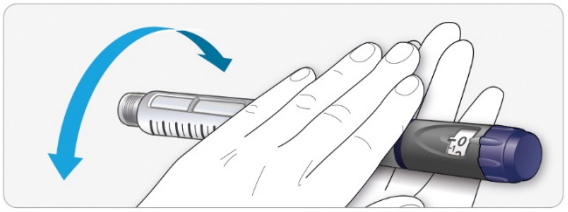
- Make sure you have the correct insulin. This is especially important if you have other injector pens.
- Never use your pen after the expiry date.

1B Pull off the pen cap.



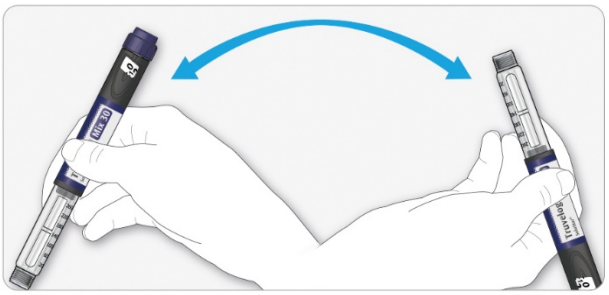
1C For every first injection roll the pen between your palms 10 times.

- Make sure that the pen is kept horizontal.



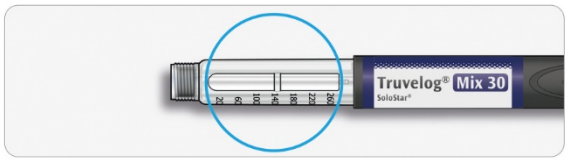
1D Then gently move the pen up and down 10 times as shown for every first injection.

- Make sure the balls inside the cartridge move from one end of the cartridge to the other.



1E Check that the insulin is uniformly white and cloudy.

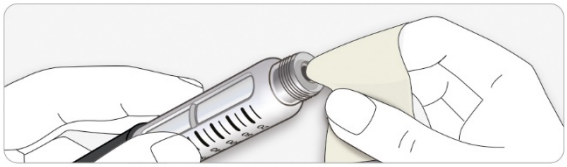
- Repeat rolling and moving the pen until the liquid appears uniformly white and cloudy.



For every following injection:

- Move the pen up and down at least 10 times as instructed for first injection (see 1D), until the liquid appears uniformly white and cloudy.
- After mixing, complete all the following steps of the injection right away. If there is a delay, the insulin will need to be mixed again.

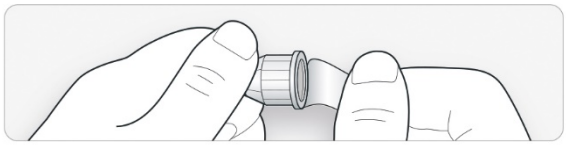
1F Wipe the rubber seal with an alcohol swab.



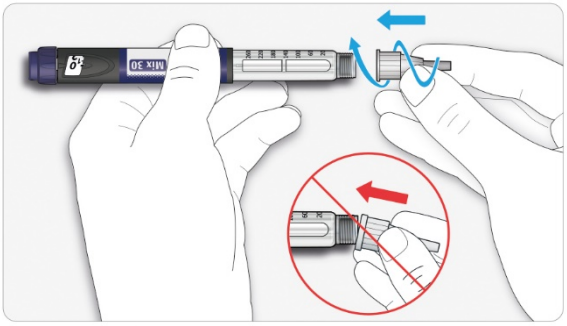
STEP 2: Attach a new needle

- 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 Truvelog Mix 30.

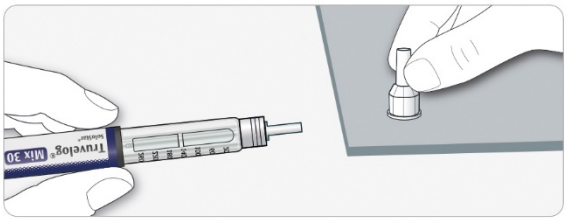
2A Take a needle and peel off the protective seal.



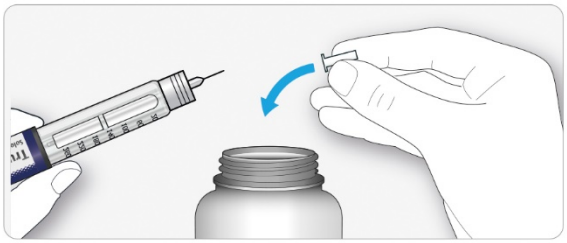
2B Keep the needle straight and screw it onto the pen until fixed. Do not overtighten.



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.

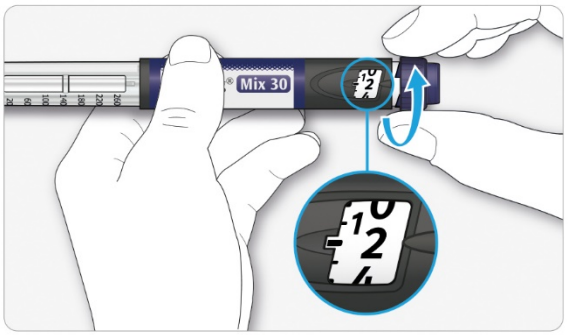
STEP 3: Do a safety test

Always do a safety test before each injection to:

- check your pen and the needle are working properly.
- make sure that you get the correct insulin dose.

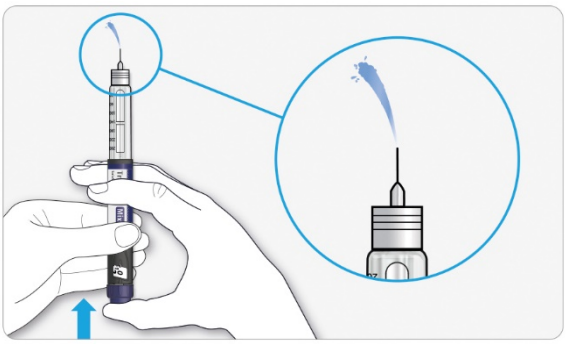
If the pen is new, you must perform safety tests before you use the pen for the first time until you see insulin coming out of the needle tip. If you see insulin coming out of the needle tip, the pen is ready to use. If you do not see insulin coming out before using your dose, you could get an underdose or no insulin at all. This could cause high blood sugar.

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.



3C 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.

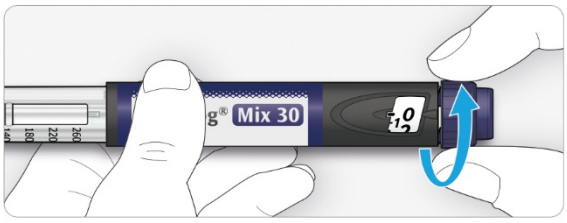
STEP 4: Select the dose

- **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:

Odd numbers are shown as a line between even numbers:

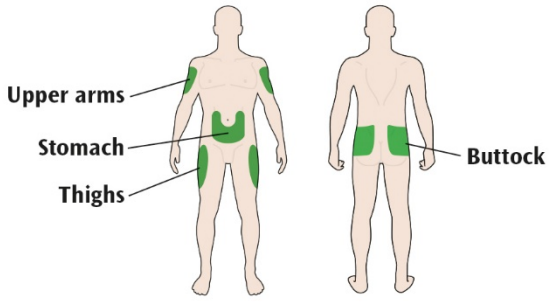
Units of insulin in your pen

- 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

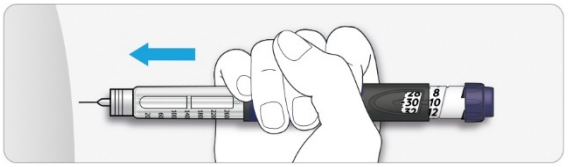
If you find it hard to press the injection button in, do not force it as this may break your pen. See the section below for help.

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



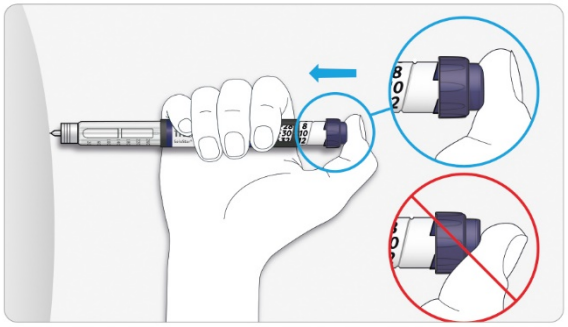
5B Push the needle into your skin as shown by your doctor, pharmacist or nurse.

- Do not touch the injection button yet.



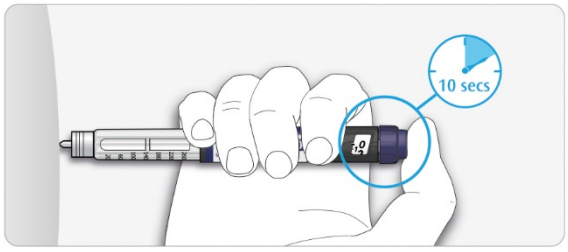
5C Place your thumb on the injection button. Then press all the way in and hold.

- **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 injection button in:

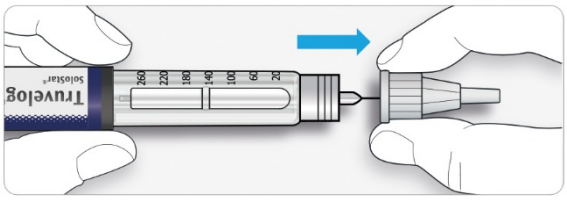
- Change the needle (see **Step 6** and **Step 2**) then do a safety test (see **Step 3**).
- If you still find it hard to press in, get a new pen.
- **Never** use a syringe to remove insulin from your pen.

STEP 6: Remove the needle from your pen

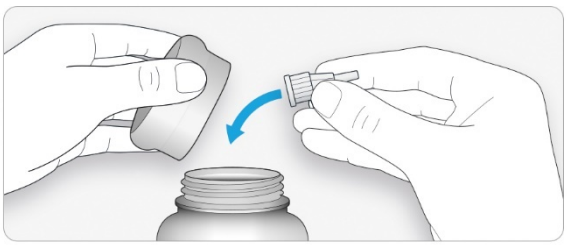
- Take care when handling needles – this is to prevent needle injury and cross-infection.
- **Never** put the inner needle cap back on.

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.

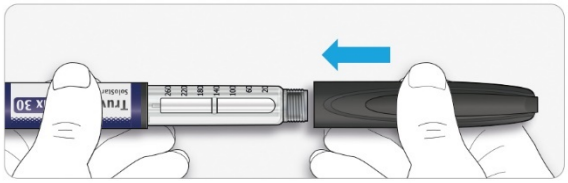


6B Throw away the used needle in a puncture resistant container, or as told by your pharmacist or local authority.



6C Put the pen cap back on.

- Do not put the pen back in the fridge.



How to store and care for your 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 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.