

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

Fiasp 100 units/mL solution for injection in pre-filled pen
Fiasp 100 units/mL solution for injection in cartridge
Fiasp 100 units/mL solution for injection in vial

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 mL of the solution contains 100 units of insulin aspart* (equivalent to 3.5 mg).

Fiasp 100 units/mL solution for injection in pre-filled pen
One pre-filled pen contains 300 units of insulin aspart in 3 mL solution.

Fiasp 100 units/mL solution for injection in cartridge
One cartridge contains 300 units of insulin aspart in 3 mL solution.

Fiasp 100 units/mL solution for injection in vial
One vial contains 1,000 units of insulin aspart in 10 mL solution.

*Insulin aspart is produced in *Saccharomyces cerevisiae* by recombinant DNA technology.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Fiasp 100 units/mL solution for injection in pre-filled pen
Solution for injection (FlexTouch).

Fiasp 100 units/mL solution for injection in cartridge
Solution for injection (Penfill).

Fiasp 100 units/mL solution for injection in vial
Solution for injection.

Clear, colourless, aqueous solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of diabetes mellitus in adults.

4.2 Posology and method of administration

Posology

Fiasp is a mealtime insulin for subcutaneous administration up to 2 minutes before the start of the meal, with the option to administer up to 20 minutes after starting the meal (see section 5.1).

Dosing with Fiasp is individual and determined in accordance with the needs of the patient. Fiasp given by subcutaneous injection should be used in combination with intermediate-acting or long-acting insulin given at least once a day. In a basal-bolus treatment regimen approximately 50% of this requirement may be provided by Fiasp and the remaining by intermediate-acting or long-acting insulin.

The individual total daily insulin requirement in adults may vary and is usually between 0.5 and 1.0 unit/kg/day.

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

Adjustment of dose may be necessary if patients undertake increased physical activity, change their usual diet or during concomitant illness. Blood glucose levels should be monitored adequately under these conditions.

The duration of action will vary according to the dose, injection site, blood flow, temperature and level of physical activity.

Patients on basal-bolus treatment who forget a mealtime dose are advised to monitor their blood glucose level to decide if an insulin dose is needed. Patients should resume their usual dosing schedule at the next meal.

The potency of insulin analogues, including Fiasp, is expressed in units. One (1) unit of Fiasp corresponds to 1 international unit of human insulin or 1 unit of other fast-acting insulin analogues.

Initiation

Patients with type 1 diabetes mellitus

The recommended starting dose in insulin naïve patients with type 1 diabetes is approximately 50% of the total daily insulin dose and should be divided between the meals based on the size and composition of the meals. The remainder of the total daily insulin dose should be administered as intermediate-acting or long-acting insulin. As a general rule, 0.2 to 0.4 units of insulin per kilogram of body weight can be used to calculate the initial total daily insulin dose in insulin naïve patients with type 1 diabetes.

Patients with type 2 diabetes mellitus

Suggested initial dose is 4 units at one or more meals. Number of injections and subsequent titration will depend on individual glycaemic target and the size and composition of the meals.

Dose adjustment may be considered daily based on self-measured plasma glucose (SMPG) on the previous day(s) according to Table 1.

- Pre-breakfast dose should be adjusted according to the pre-lunch SMPG the previous day
- Pre-lunch dose should be adjusted according to the pre-dinner SMPG the previous day
- Pre-dinner dose should be adjusted according to the bedtime SMPG the previous day

Table 1 Dose adjustment

SMPG (see above)		Dose adjustment
mmol/L	mg/dL	Unit
<4.0	<71	-1
4.0–6.0	71–108	No adjustment
>6.0	>108	+1

Special populations

Elderly patients (≥ 65 years old)

The safety and efficacy of Fiasp has been established in elderly patients aged 65 to 75 years. Close glucose monitoring is recommended and the insulin dose should be adjusted on an individual basis (see section 5.1 and 5.2). The therapeutic experience in patients ≥ 75 years of age is limited.

Renal and hepatic impairment

Renal or hepatic impairment may reduce the patient's insulin requirements. In patients with renal or hepatic impairment, glucose monitoring should be intensified and the dose adjusted on an individual basis (see section 5.2).

Paediatric population

The safety and efficacy of Fiasp in children and adolescents below 18 years of age have not been established. Currently available data are described in section 5.2, but no recommendation on a posology can be made.

Transfer from other insulin medicinal products

Close glucose monitoring is recommended during the transfer from other mealtime insulins and in the initial weeks thereafter. Converting from another mealtime insulin can be done on a unit-to-unit basis. Transferring a patient from another type, brand or manufacturer of insulin to Fiasp must be done under medical supervision and may result in the need for a change in dosage.

Doses and timing of concurrent intermediate-acting or long-acting insulin medicinal products or other concomitant antidiabetic treatment may need to be adjusted.

Method of administration

Subcutaneous injection

Fiasp is recommended to be administered subcutaneously in the abdominal wall or the upper arm (see section 5.2). Injection sites should be rotated within the same region in order to reduce the risk of lipodystrophy.

Continuous subcutaneous insulin infusion (CSII)

Fiasp can be used for CSII in pumps suitable for insulin infusion and will cover both the bolus insulin requirement (approximately 50%) and basal insulin. It can be administered in accordance with the instructions provided by the pump manufacturer, preferably in the abdomen. Infusion site should be rotated within the same region to reduce the risk of lipodystrophy. When used with an insulin infusion pump, it should not be diluted or mixed with any other insulin medicinal products.

Patients using CSII should be instructed in the use of the pump and use the correct reservoir and tubing for pump (see section 6.6). The infusion set (tubing and cannula) should be changed in accordance with the instructions in the product information supplied with the infusion set.

Patients administering Fiasp by CSII must be trained to administer insulin by injection and have alternate insulin therapy available in case of pump failure.

Intravenous use

If necessary, Fiasp can be administered intravenously by health care professionals.

For intravenous use, it should be used at concentrations from 0.5 unit/mL to 1.0 unit/mL insulin aspart in infusion systems – using polypropylene infusion bags. Fiasp has been shown to be stable at room temperature for 24 hours in the infusion fluids such as sodium chloride 9 mg/mL (0.9%) solution or 5% glucose solution.

Monitoring of blood glucose is necessary during insulin infusion. Care should be taken to ensure that the insulin is injected into the infusion bag and not simply the entry port.

Fiasp 100 units/mL solution for injection in pre-filled pen

Administration with a pre-filled pen (FlexTouch)

The pre-filled pen (FlexTouch) is designed to be used with NovoFine Plus, NovoFine or NovoTwist injection needles. The pre-filled pen delivers 1–80 units in steps of 1 unit.

FlexTouch is colour-coded yellow and accompanied by a package leaflet with detailed instructions for use to be followed.

Fiasp 100 units/mL solution for injection in cartridge

Administration with an insulin delivery system

The cartridge (Penfill) is designed to be used with Novo Nordisk insulin delivery systems and NovoFine Plus, NovoFine or NovoTwist injection needles.

Fiasp 100 units/mL solution for injection in vial

Administration with a syringe

The vial is to be used with insulin syringes with the corresponding unit scale (U-100 or 100 U/mL).

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

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 (see sections 4.8 and 4.9).

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

The timing of hypoglycaemia usually reflects the time-action profile of the administered insulin formulation. Hypoglycaemia may occur earlier after an injection/infusion when compared to other mealtime insulins due to the earlier onset of action of Fiasp (see section 5.1).

Since Fiasp should be administered up to 2 minutes before the start of the meal with the option to administer up to 20 minutes after starting the meal, the time to onset of action must be taken into account when prescribing to patients with concomitant diseases or treatment where a delayed absorption of food might be expected.

Hyperglycaemia

The use of inadequate doses or discontinuation of treatment, especially in patients requiring insulin, may lead to hyperglycaemia and diabetic ketoacidosis; conditions which are potentially lethal.

Continuous subcutaneous insulin infusion (CSII)

Pump or infusion set malfunctions can lead to a fast onset of hyperglycaemia and ketosis. Prompt identification and correction of the cause of hyperglycaemia or ketosis is necessary. Interim therapy with subcutaneous injection may be required.

Concomitant illness

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 may require changes in the insulin dose.

Combination of thiazolidinediones and insulin medicinal products

Cases of congestive heart failure have been reported when thiazolidinediones were used in combination with insulin, especially in patients with risk factors for development of congestive heart failure. This should be kept in mind if treatment with the combination of thiazolidinediones and insulin medicinal products is considered. If the combination is used, patients should be observed for

signs and symptoms of congestive heart failure, weight gain and oedema. Thiazolidinediones should be discontinued if any deterioration in cardiac symptoms occurs.

Insulin initiation and glucose control intensification

Intensification or rapid improvement in glucose control has been associated with a transitory, reversible ophthalmologic refraction disorder, worsening of diabetic retinopathy, acute painful peripheral neuropathy, and peripheral oedema. However, long-term glycaemic control decreases the risk of diabetic retinopathy and neuropathy.

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.

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 this medicinal product and other insulin medicinal products.

Patients must visually verify the units of the dose prior to administering. Therefore, the requirement for patients to self-administer is that they can read the dose scale. Patients, who are blind or have poor vision, must be instructed to always get assistance from another person who has good vision and is trained in administration of insulins.

Travelling between time zones

Before travelling between different time zones, the patient should seek the doctor's advice.

Excipients

This medicinal product contains less than 1 mmol sodium (23 mg) per dose i.e. 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 insulin requirement:

Oral antidiabetics, monoamine oxidase inhibitors (MAOIs), beta-blockers, angiotensin converting enzyme (ACE) inhibitors, salicylates, anabolic steroids, sulphonamides and GLP-1 receptor agonist.

The following substances may increase insulin requirement:

Oral contraceptives, thiazides, glucocorticoids, thyroid hormones, sympathomimetics, growth hormone and danazol.

Beta-blocking agents 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

Fiasp can be used in pregnancy.

Data from two randomised controlled clinical trials conducted with insulin aspart (322 + 27 exposed pregnancies) do not indicate any adverse effect of insulin aspart on pregnancy or on the health of the foetus/new born when compared to soluble human insulin.

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

Breast-feeding

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

Fertility

Animal reproduction studies have not revealed any differences between insulin aspart and human insulin regarding fertility.

4.7 Effects on ability to drive and use machines

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

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

4.8 Undesirable effects

Summary of safety profile

The most frequently reported adverse reaction during treatment is hypoglycaemia (see section 'Description of selected adverse reactions' below).

Tabulated list of adverse reactions

Adverse reactions listed below (Table 2) are based on clinical trial data from phase 3 trials consisting of 4 completed therapeutic confirmatory trials. Frequency categories are defined according to the following convention: Very common ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1,000$ to $< 1/100$); rare ($\geq 1/10,000$ to $< 1/1,000$); very rare ($< 1/10,000$) and not known (cannot be estimated from the available data).

Table 2 Adverse reactions from clinical trials

MedDRA System Organ Class	Very common	Common	Uncommon
Immune system disorders			Hypersensitivity
Metabolism and nutrition disorders	Hypoglycaemia		
Skin and subcutaneous tissue disorders		Allergic skin manifestations	Lipodystrophy
General disorders and administration site conditions		Injection/infusion site reactions	

Description of selected adverse reactions

Allergic reactions

Allergic skin manifestations reported with Fiasp (1.5% vs. 1.4% for comparator) include eczema, rash, rash pruritic, urticaria and dermatitis.

With Fiasp generalised hypersensitivity reactions (manifested by generalised skin rash and facial oedema) was reported uncommonly (0.2% vs. 0.1% for comparator). Anaphylactic reactions have not been reported with Fiasp. With insulin preparations in general, anaphylactic reactions may occur. Immediate-type allergic reactions to either insulin itself or the excipients may potentially be life-threatening.

Hypoglycaemia

Hypoglycaemia may occur if the insulin dose is too high in relation to the insulin requirement. Severe hypoglycaemia may lead to unconsciousness and/or convulsions and may result in temporary or permanent impairment of brain function or even death. The symptoms of hypoglycaemia usually occur suddenly. They may include cold sweats, cool pale skin, fatigue, nervousness or tremor, anxiousness, unusual tiredness or weakness, confusion, difficulty in concentration, drowsiness, excessive hunger, vision changes, headache, nausea and palpitation (see section 4.4 and 5.1). Hypoglycaemia may occur earlier after an injection/infusion of Fiasp compared to other mealtime insulins due to the earlier onset of action.

Lipodystrophy

Lipodystrophy (including lipohypertrophy, lipoatrophy) was reported at the injection/infusion site in patients treated with Fiasp (0.2% vs. 0% in comparator). Continuous rotation of the injection site within the particular injection area may help to reduce the risk of developing these reactions.

Injection/infusion site reactions

Injection/infusion site reactions (including rash, redness, inflammation, bruising, and itching) was reported in patients treated with Fiasp (1.0% vs. 0.7% in comparator). These reactions are usually mild and transitory and they normally disappear during continued treatment.

Special populations

Based on results from clinical trials with insulin aspart in general, 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. The safety profile in very elderly patients (≥ 75 years) or patients with moderate to severe renal impairment or hepatic impairment is limited. Fiasp has been administered to elderly patients for the investigation of pharmacokinetic properties (see section 5.2).

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 a patient is dosed with more insulin than required:

- Mild hypoglycaemic episodes can be treated by oral administration of glucose or other products containing sugar. It is therefore recommended that the diabetic patient always carries glucose-containing products.

- Severe hypoglycaemic episodes, where the patient is not able to treat him/herself, can be treated with glucagon (0.5 to 1 mg) given intramuscularly or subcutaneously by a trained person, or with glucose given intravenously by a healthcare professional. Glucose must be given intravenously if the patient does not respond to glucagon within 10 to 15 minutes. Upon regaining consciousness, administration of oral carbohydrate is recommended for the patient in order to prevent a relapse.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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

Mechanism of action

Fiasp is a fast-acting insulin aspart formulation.

The primary activity of Fiasp is the regulation of glucose metabolism. Insulins, including insulin aspart, the active ingredient in Fiasp, exert their specific action through binding to insulin receptors. Receptor-bound insulin lowers blood glucose by facilitating cellular uptake of glucose into skeletal muscle and adipose tissue and by inhibiting the output of glucose from the liver. Insulin inhibits lipolysis in the adipocyte, inhibits proteolysis, and enhances protein synthesis.

Pharmacodynamic effects

Fiasp is a mealtime insulin aspart formulation in which the addition of nicotinamide (vitamin B₃) results in a faster initial absorption of insulin compared to NovoRapid.

The onset of action was 5 minutes earlier and time to maximum glucose infusion rate was 11 minutes earlier with Fiasp than with NovoRapid. The maximum glucose-lowering effect of Fiasp occurred between 1 and 3 hours after injection. The glucose-lowering effect during the first 30 minutes ($AUC_{GIR, 0-30 \text{ min}}$) was 51 mg/kg with Fiasp and 29 mg/kg with NovoRapid (Fiasp/NovoRapid ratio: 1.74 [1.47;2.10]_{95% CI}). The total glucose-lowering effect and maximum (GIR_{max}) glucose-lowering effect were comparable between Fiasp and NovoRapid. Total and maximum glucose-lowering effect of Fiasp increase linearly with increasing dose within the therapeutic dose range.

The duration of action was shorter for Fiasp compared to that of NovoRapid, and lasts for 3–5 hours.

The day-to-day variability within-patients in glucose-lowering effect was low for Fiasp both for early ($AUC_{GIR, 0-1h}$, CV~26%), total ($AUC_{GIR, 0-12h}$, CV~18%) and maximum glucose-lowering effect (GIR_{max} , CV~19%).

Clinical efficacy and safety

Fiasp has been studied in 2,068 randomised adult patients with type 1 diabetes mellitus (1,143 patients) and type 2 diabetes mellitus (925 patients) in 3 efficacy and safety trials (18–26 weeks of treatment).

Patients with type 1 diabetes mellitus

The treatment effect of Fiasp in achieving glycaemic control was assessed when administered at mealtime or postmeal. Fiasp administered at mealtime was non-inferior to NovoRapid in reducing HbA_{1c}, and the improvement in HbA_{1c} was statistically significant in favour of Fiasp. Fiasp administered postmeal achieved similar HbA_{1c} reduction as NovoRapid dosed at mealtime (Table 3).

Table 3 Results from 26 week basal-bolus clinical trial in patients with type 1 diabetes

	Fiasp mealtime + insulin detemir	Fiasp postmeal + insulin detemir	NovoRapid mealtime + insulin detemir
N	381	382	380
HbA_{1c} (%)			
Baseline → End of trial	7.6 → 7.3	7.6 → 7.5	7.6 → 7.4
Adjusted change from baseline	-0.32	-0.13	-0.17
Estimated treatment difference	-0.15 [-0.23;-0.07] ^{CE}	0.04 [-0.04;0.12] ^D	
HbA_{1c} (mmol/mol)			
Baseline → End of trial	59.7 → 56.4	59.9 → 58.6	59.3 → 57.6
Adjusted change from baseline	-3.46	-1.37	-1.84
Estimated treatment difference	-1.62 [-2.50;-0.73] ^{CE}	0.47[-0.41;1.36] ^D	
2-hour postmeal glucose increment (mmol/L)^A			
Baseline → End of trial	6.1 → 5.9	6.1 → 6.7	6.2 → 6.6
Adjusted change from baseline	-0.29	0.67	0.38
Estimated treatment difference	-0.67 [-1.29;-0.04] ^{CE}	0.30 [-0.34;0.93] ^D	
1-hour postmeal glucose increment (mmol/L)^A			
Baseline → End of trial	5.4 → 4.7	5.4 → 6.6	5.7 → 5.9
Adjusted change from baseline	-0.84	1.27	0.34
Estimated treatment difference	-1.18[-1.65;-0.71] ^{CE}	0.93[0.46;1.40] ^D	
Bodyweight (kg)			
Baseline → End of trial	78.6 → 79.2	80.5 → 81.2	80.2 → 80.7
Adjusted change from baseline	0.67	0.70	0.55
Estimated treatment difference	0.12 [-0.30;0.55] ^C	0.16 [-0.27;0.58] ^D	
Observed rate of severe or BG confirmed hypoglycaemia^B per patient year of exposure (percentage of patients)	59.0 (92.7)	54.4 (95.0)	58.7 (97.4)
Estimated rate ratio	1.01 [0.88;1.15] ^C	0.92 [0.81;1.06] ^D	

Baseline, End of trial values are based on the mean of the observed last available values. The 95% confidence interval is stated in '[]'

^A Meal test

^B Severe hypoglycaemia (episode requiring assistance of another person) or blood glucose (BG) confirmed hypoglycaemia defined as episodes confirmed by plasma glucose < 3.1 mmol/L irrespective of symptoms

^C The difference is for Fiasp mealtime – NovoRapid mealtime

^D The difference is for Fiasp postmeal – NovoRapid mealtime

^E Statistically significant in favour of Fiasp mealtime

33.3% of patients treated with mealtime Fiasp reached a target HbA_{1c} of < 7% compared to 23.3% of patients treated with postmeal Fiasp and 28.2% of patients treated with mealtime NovoRapid. The estimated odds of achieving HbA_{1c} < 7% were statistically significantly greater with mealtime Fiasp than with mealtime NovoRapid (odds ratio: 1.47 [1.02; 2.13]_{95% CI}). No statistical significant difference was shown between postmeal Fiasp and mealtime NovoRapid.

Fiasp administered at mealtime provided significantly lower 1-hour and 2-hour postmeal glucose increment compared to NovoRapid administered at mealtime. Fiasp administered postmeal resulted in higher 1-hour postmeal glucose increment and comparable 2-hour postmeal glucose increment to NovoRapid dosed at mealtime (Table 3).

Median total bolus insulin dose at trial end was similar for mealtime Fiasp, postmeal Fiasp and mealtime NovoRapid (change from baseline to end of trial: mealtime Fiasp: 0.33→0.39 units/kg/day; postmeal Fiasp: 0.35→0.39 units/kg/day; and mealtime NovoRapid: 0.36→0.38 units/kg/day). Changes in median total basal insulin dose from baseline to end of trial were comparable for mealtime Fiasp (0.41→0.39 units/kg/day), postmeal Fiasp (0.43→0.42 units/kg/day) and mealtime NovoRapid (0.43→0.43 units/kg/day).

Patients with type 2 diabetes mellitus

The reduction in HbA_{1c} from baseline to end of trial was confirmed to be non-inferior to that obtained with NovoRapid (Table 4).

Table 4 Results from 26 week basal-bolus clinical trial in patients with type 2 diabetes

	Fiasp + insulin glargine	NovoRapid + insulin glargine
N	345	344
HbA_{1c} (%)		
Baseline → End of trial	8.0 → 6.6	7.9 → 6.6
Adjusted change from baseline	-1.38	-1.36
<i>Estimated treatment difference</i>		-0.02[-0.15;0.10]
HbA_{1c} (mmol/mol)		
Baseline → End of trial	63.5 → 49.0	62.7 → 48.6
Adjusted change from baseline	-15.10	-14.86
<i>Estimated treatment difference</i>		-0.24 [-1.60;1.11]
2-hour postmeal glucose increment (mmol/L)^A		
Baseline → End of trial	7.6 → 4.6	7.3 → 4.9
Adjusted change from baseline	-3.24	-2.87
<i>Estimated treatment difference</i>		-0.36 [-0.81;0.08]
1-hour postmeal glucose increment (mmol/L)^A		
Baseline → End of trial	6.0 → 4.1	5.9 → 4.6
Adjusted change from baseline	-2.14	-1.55
<i>Estimated treatment difference</i>		-0.59 [-1.09;-0.09] ^c
Bodyweight (kg)		
Baseline → End of trial	89.0 → 91.6	88.3 → 90.8
Adjusted change from baseline	2.68	2.67
<i>Estimated treatment difference</i>		0.00 [-0.60;0.61]
Observed rate of severe or BG confirmed hypoglycaemia^B per patient year of exposure (percentage of patients)		
<i>Estimated rate ratio</i>	17.9 (76.8)	16.6 (73.3)
		1.09 [0.88;1.36]

Baseline, End of trial values are based on the mean of the observed last available values. The 95% confidence interval is stated in '[]'

^A Meal test

^B Severe hypoglycaemia (episode requiring assistance of another person) or blood glucose (BG) confirmed hypoglycaemia defined as episodes confirmed by plasma glucose < 3.1 mmol/L irrespective of symptoms

^C Statistically significant in favour of Fiasp

Postmeal dosing has not been investigated in patients with type 2 diabetes mellitus.

74.8% of patients treated with Fiasp reached a target HbA_{1c} of < 7% compared to 75.9% of patients treated with NovoRapid. There was no statistical significant difference between Fiasp and NovoRapid in the estimated odds of achieving HbA_{1c} < 7%.

Median total bolus insulin dose at trial end was similar for Fiasp and NovoRapid (change from baseline to end of trial: Fiasp: 0.21→0.49 units/kg/day and NovoRapid: 0.21→0.51 units/kg/day). Changes in median total basal insulin dose from baseline to end of trial were comparable for Fiasp (0.56→0.53 units/kg/day) and NovoRapid (0.52→0.48 units/kg/day).

Elderly

In the three controlled clinical studies, 192 of 1,219 (16%) Fiasp treated patients with type 1 diabetes mellitus or type 2 diabetes mellitus were ≥ 65 years of age and 24 of 1,219 (2%) were ≥ 75 years of age. No overall differences in safety or effectiveness were observed between elderly patients and younger patients.

Continuous subcutaneous insulin infusion (CSII)

A 6-week, randomised (2:1), double-blind, parallel-group, active controlled trial evaluated compatibility of Fiasp and NovoRapid administered via CSII system in adult patients with type 1 diabetes. There were no microscopically confirmed episodes of infusion set occlusions in either the

Fiasp (N=25) or NovoRapid (N=12) groups. There were two patients from the Fiasp group who each reported two treatment-emergent infusion site reactions.

In a 2-week cross-over trial, Fiasp showed a greater postmeal glucose-lowering effect after a standardised meal test with regard to 1-hour and 2-hour postmeal glucose response (treatment difference: -0.50 mmol/L [-1.07; 0.07]_{95% CI} and -0.99 mmol/L [-1.95; -0.03]_{95% CI}), respectively compared to NovoRapid in a CSII setting.

5.2 Pharmacokinetic properties

Absorption

Fiasp is a mealtime insulin aspart formulation in which the addition of nicotinamide (vitamin B₃) results in a faster initial absorption of insulin. Insulin appeared in the circulation approximately 4 minutes after administration (Figure 1). The onset of appearance was twice as fast (corresponding to 5 minutes earlier), time to 50% maximum concentration was 9 minutes shorter with Fiasp compared to NovoRapid with four times as much insulin available during first 15 minutes and with twice as much insulin available during the first 30 minutes.

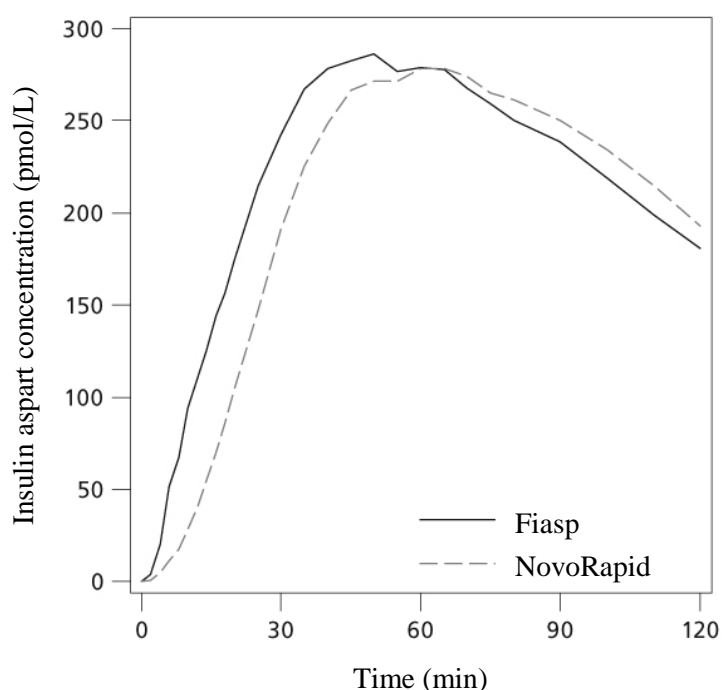


Figure 1 Mean insulin profile in patients with type 1 diabetes after subcutaneous injection.

The total insulin exposure was comparable between Fiasp and NovoRapid. The mean C_{max} for a dose of 0.2 units/kg body weight is 298 pmol/L and comparable to NovoRapid.

Total exposure and maximum insulin concentration increases proportionally with increasing subcutaneous dose of Fiasp within the therapeutic dose range.

The absolute bioavailability of insulin aspart after subcutaneous administration of Fiasp in the abdomen, deltoid and thigh was approximately 80%.

After administration of Fiasp, the fast onset of appearance is maintained regardless of injection site. Time to maximum concentration and total insulin aspart exposure were all comparable between the abdomen, upper arm and the thigh. Early insulin exposure and maximum concentration were comparable for the abdomen and upper arm regions, but lower for the thigh.

Continuous subcutaneous insulin infusion (CSII)

The onset of exposure in a CSII setting (time to reach maximum concentration) was 26 minutes shorter with Fiasp compared to NovoRapid resulting in approximately three times as much insulin available during the first 30 minutes (Figure 2).

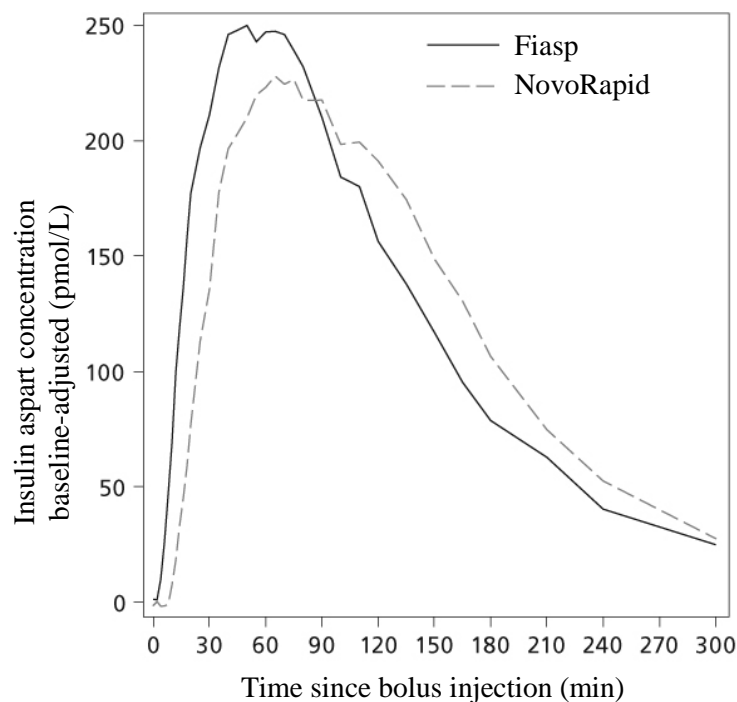


Figure 2 Mean insulin profiles in patients with type 1 diabetes in a CSII setting (0–5 hours) corrected for basal insulin infusion

Distribution

Insulin aspart has a low binding affinity to plasma proteins (< 10%), similar to that seen with regular human insulin.

Volume of distribution (V_d) after intravenous administration was 0.22 L/kg (e.g., 15.4 L for a 70 kg subject) corresponding to the extracellular fluid volume in the body.

Biotransformation

Degradation of insulin aspart is similar to that of human insulin; all metabolites formed are inactive.

Elimination

Half-life after subcutaneous administration of Fiasp is 57 minutes and comparable to NovoRapid.

Following intravenous administration of Fiasp, clearance was rapid (1.0 L/h/kg) and the elimination half-life was 10 minutes.

Special populations

Elderly

In elderly patients with type 1 diabetes Fiasp showed, an earlier onset of exposure and a higher early insulin exposure whilst maintaining a similar total exposure and maximum concentration compared to NovoRapid.

Total insulin aspart exposure and maximum concentration following administration of Fiasp was 30% higher in elderly subjects compared to younger adult subjects.

Gender

The effect of gender on the pharmacokinetics of Fiasp was examined in an across-trial analysis of the pharmacokinetic studies. Fiasp showed a comparable earlier onset of exposure and a higher early insulin exposure whilst maintaining a similar total exposure and maximum concentration compared to NovoRapid for both females and male patients with type 1 diabetes.

The early and maximum insulin exposure of Fiasp was comparable for female and male patients with type 1 diabetes. However, total insulin exposure was larger in female compared to male patients with type 1 diabetes.

Obesity

The initial absorption rate was slower with increasing BMI while the total exposure was similar across different BMI levels. Compared to NovoRapid, the influence of BMI on the absorption was less pronounced for Fiasp leading to relatively higher initial exposure.

Race and Ethnicity

The effect of race and ethnicity (Blacks versus Whites and Hispanics versus non-Hispanics) on the total insulin exposure of Fiasp was based on results from a population pharmacokinetic analysis in patients with type 1 diabetes. For Fiasp no difference in exposure was found between the racial and ethnic groups investigated.

Hepatic impairment

A single dose pharmacokinetic study of insulin aspart was performed with NovoRapid in 24 subjects with hepatic function ranging from normal to severely impaired. In subjects with hepatic impairment, absorption rate was decreased and more variable.

Renal impairment

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

Paediatric population

In children (6–11 years) and adolescents (12–18 years) Fiasp showed, an earlier onset of exposure and a higher early insulin exposure whilst maintaining a similar total exposure and maximum concentration compared to NovoRapid.

Onset and early insulin exposure of Fiasp was similar in children and adolescents to that in adults. Total exposure of Fiasp was lower in children and adolescents compared to adults when dosed with 0.2 units/kg body weight, while the maximum serum insulin aspart concentration was similar between age groups.

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

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Phenol
Metacresol
Glycerol
Zinc acetate
Disodium phosphate dihydrate
Arginine hydrochloride
Nicotinamide (vitamin B₃)
Hydrochloric acid (for pH adjustment)
Sodium hydroxide (for pH adjustment)
Water for injections

6.2 Incompatibilities

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

6.3 Shelf life

30 months.

Fiasp 100 units/mL solution for injection in pre-filled pen

After first opening or carried as a spare, the medicinal product may be stored for a maximum of 4 weeks. At the end of this period the pen should be used or discarded. Do not store above 30°C. Can be stored in the refrigerator (2°C–8°C). Do not freeze. Keep the cap on the pen in order to protect from light.

Fiasp 100 units/mL solution for injection in cartridge

After first opening or carried as a spare, the medicinal product may be stored for a maximum of 4 weeks. At the end of this period the cartridge should be used or discarded. Do not store above 30°C. Do not refrigerate. Do not freeze. If cartridge is carried as a spare and unused, the cartridge should be kept in the outer carton in order to protect from light.

Fiasp 100 units/mL solution for injection in vial

After first opening, the medicinal product may be stored for a maximum of 4 weeks. At the end of this period the vial should be used or discarded. Do not store above 30°C. Can be stored in the refrigerator (2°C–8°C). Do not freeze. Keep the vial in outer carton in order to protect from light.

6.4 Special precautions for storage

Fiasp 100 units/mL solution for injection in pre-filled pen

Store in a refrigerator (2°C–8°C). Do not freeze. Keep away from the freezing element. Keep the cap on the pen in order to protect from light.

Fiasp 100 units/mL solution for injection in cartridge

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

Fiasp 100 units/mL solution for injection in vial

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

After first opening or carried as a spare, see section 6.3.

6.5 Nature and contents of container

Fiasp 100 units/mL solution for injection in pre-filled pen

Cartridge (type 1 glass) with a plunger (halobutyl) and a stopper (halobutyl/polyisoprene) contained in a pre-filled multidose disposable pen made of polypropylene, polyoxymethylene, polycarbonate and acrylonitrile butadiene styrene.

Each pre-filled pen contains 3 mL of solution.

Pack sizes of 1 (with and without needles) pre-filled pen, 5 (without needles) pre-filled pens and multipack containing 10 (2 packs of 5) (without needles) pre-filled pens.

Fiasp 100 units/mL solution for injection in cartridge

Cartridge (type 1 glass), with a plunger (halobutyl) and a stopper (halobutyl/polyisoprene) in a carton.

Each cartridge contains 3 mL of solution.

Pack sizes of 5 and 10 cartridges.

Fiasp 100 units/mL solution for injection in vial

Vial (type 1 glass) closed with a halobutyl/polyisoprene rubber disc and a protective plastic cap in order to obtain a tamper-proof container in a carton.

Each vial contains 10 mL of solution.

Pack sizes of 1 vial, 5 vials and a multipack containing 5 (5 packs of 1) vials.

6.6 Special precautions for disposal and other handling

Fiasp must not be used if the solution does not appear clear and colourless.

Fiasp which has been frozen must not be used.

The patient should discard the needle after each injection.

Fiasp 100 units/mL solution for injection in pre-filled pen

Needles and pre-filled pens must not be shared. The cartridge must not be refilled.

In case of emergency in patients already using Fiasp (hospitalisation or insulin pen malfunction), Fiasp can be withdrawn with an U100 insulin syringe from a FlexTouch pen.

Fiasp 100 units/mL solution for injection in cartridge

Needles and cartridges must not be shared. The cartridge must not be refilled.

In case of emergency in current Fiasp users (hospitalisation or insulin pen malfunction), Fiasp can be withdrawn with an U100 insulin syringe from a cartridge.

Fiasp 100 units/mL solution for injection in vial

Needles and syringes must not be shared.

Fiasp may be used in an infusion pump (CSII) for a maximum of 9 days, as described in section 4.2 and in the package leaflet. Tubings in which the inner surface materials are made of polyethylene or polyolefin have been evaluated and found compatible with pump use.

Disposal

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

7. MARKETING AUTHORISATION HOLDER

Novo Nordisk A/S
Novo Allé
DK-2880 Bagsværd
Denmark

8. MARKETING AUTHORISATION NUMBERS

EU/1/16/1160/001
EU/1/16/1160/002
EU/1/16/1160/003
EU/1/16/1160/004
EU/1/16/1160/005
EU/1/16/1160/006
EU/1/16/1160/007
EU/1/16/1160/008
EU/1/16/1160/009
EU/1/16/1160/010
EU/1/16/1160/011

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: {DD month YYYY}

10. DATE OF REVISION OF THE TEXT

{MM/YYYY}
{DD/MM/YYYY}
{DD month YYYY}

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 MANUFACTURER 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
MANUFACTURER RESPONSIBLE FOR BATCH RELEASE**

Name and address of the manufacturer of the biological active substance

Novo Nordisk A/S
Hallas Alle
4400 Kalundborg
DENMARK

Name and address of the manufacturer responsible for batch release

Novo Nordisk A/S
Novo Alle 1
2880 Bagsværd
DENMARK

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

**C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING
AUTHORISATION**

- Periodic safety update reports

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

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

- Risk Management Plan (RMP)

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

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

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (Pre-filled pen (FlexTouch))

1. NAME OF THE MEDICINAL PRODUCT

Fiasp 100 units/mL solution for injection in pre-filled pen
insulin aspart

2. STATEMENT OF ACTIVE SUBSTANCE

One pre-filled pen contains 300 units of insulin aspart in 3 mL solution
1 mL solution contains 100 units of insulin aspart (equivalent to 3.5 mg)

3. LIST OF EXCIPIENTS

phenol, metacresol, glycerol, zinc acetate, disodium phosphate dihydrate, arginine hydrochloride, nicotinamide (vitamin B₃), hydrochloric acid/sodium hydroxide (for pH adjustment) and water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

FlexTouch

1 x 3 mL

1 x 3 mL + 7 NovoFine Plus needles

1 x 3 mL + 7 NovoFine needles

1 x 3 mL + 7 NovoTwist needles

5 x 3 mL

5. METHOD AND ROUTES OF ADMINISTRATION

Needles are not included

Read the package leaflet before use

Subcutaneous or intravenous use

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

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNINGS, IF NECESSARY

Use only clear, colourless solution

Single patient use only

Designed to be used with NovoFine Plus, NovoFine or NovoTwist disposable needles up to a length of 8 mm

8. EXPIRY DATE

EXP

During use: Use within 4 weeks

9. SPECIAL STORAGE CONDITIONS

Before opening: Store in a refrigerator. Do not freeze

During use: Can be stored in the refrigerator. Store below 30°C. Do not freeze. Keep the 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

Discard the needle after each injection

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novo Nordisk A/S
Novo Allé
DK-2880 Bagsværd
Denmark

12. MARKETING AUTHORISATION NUMBER

EU/1/16/1160/001 1 pen of 3 mL
EU/1/16/1160/002 1 pen of 3 mL and 7 NovoFine Plus needles
EU/1/16/1160/003 1 pen of 3 mL and 7 NovoFine needles
EU/1/16/1160/004 1 pen of 3 mL and 7 NovoTwist needles
EU/1/16/1160/005 5 pens of 3 mL

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

Fiasp

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 (FlexTouch))

1. NAME OF THE MEDICINAL PRODUCT AND ROUTES OF ADMINISTRATION

Fiasp 100 units/mL solution for injection
insulin aspart
SC, IV

2. METHOD OF ADMINISTRATION

FlexTouch

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Batch

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3 mL

6. OTHER

Novo Nordisk A/S

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON FOR MULTIPACK (Pre-filled pen (FlexTouch) - with blue box)

1. NAME OF THE MEDICINAL PRODUCT

Fiasp 100 units/mL solution for injection in pre-filled pen
insulin aspart

2. STATEMENT OF ACTIVE SUBSTANCE

One pre-filled pen contains 300 units of insulin aspart in 3 mL solution
1 mL solution contains 100 units of insulin aspart (equivalent to 3.5 mg)

3. LIST OF EXCIPIENTS

phenol, metacresol, glycerol, zinc acetate, disodium phosphate dihydrate, arginine hydrochloride, nicotinamide (vitamin B₃), hydrochloric acid/sodium hydroxide (for pH adjustment) and water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

FlexTouch

Multipack: 10 (2 packs of 5 x 3 mL)

5. METHOD AND ROUTES OF ADMINISTRATION

Needles are not included

Read the package leaflet before use

Subcutaneous or intravenous use

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

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNINGS, IF NECESSARY

Use only clear, colourless solution

Single patient use only

Designed to be used with NovoFine Plus, NovoFine or NovoTwist disposable needles up to a length of 8 mm

8. EXPIRY DATE

EXP

During use: Use within 4 weeks

9. SPECIAL STORAGE CONDITIONS

Before opening: Store in a refrigerator. Do not freeze

During use: Can be stored in the refrigerator. Store below 30°C. Do not freeze. Keep the 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

Discard the needle after each injection

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novo Nordisk A/S
Novo Allé
DK-2880 Bagsværd
Denmark

12. MARKETING AUTHORISATION NUMBER

EU/1/16/1160/006 10 pens of 3 mL

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Fiasp

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:

SN:
NN:

PARTICULARS TO APPEAR ON THE INNER PACKAGING

CARTON FOR MULTIPACK (Pre-filled pen (FlexTouch) – without blue box)

1. NAME OF THE MEDICINAL PRODUCT

Fiasp 100 units/mL solution for injection in pre-filled pen
insulin aspart

2. STATEMENT OF ACTIVE SUBSTANCE

One pre-filled pen contains 300 units of insulin aspart in 3 mL solution
1 mL solution contains 100 units of insulin aspart (equivalent to 3.5 mg)

3. LIST OF EXCIPIENTS

phenol, metacresol, glycerol, zinc acetate, disodium phosphate dihydrate, arginine hydrochloride, nicotinamide (vitamin B₃), hydrochloric acid/sodium hydroxide (for pH adjustment) and water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

FlexTouch

5 x 3 mL. Component of a multipack, cannot be sold separately

5. METHOD AND ROUTES OF ADMINISTRATION

Needles are not included
Read the package leaflet before use
Subcutaneous or intravenous use

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

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNINGS, IF NECESSARY

Use only clear, colourless solution
Single patient use only
Designed to be used with NovoFine Plus, NovoFine or NovoTwist disposable needles up to a length of 8 mm

8. EXPIRY DATE

EXP

During use: Use within 4 weeks

9. SPECIAL STORAGE CONDITIONS

Before opening: Store in a refrigerator. Do not freeze

During use: Can be stored in the refrigerator. Store below 30°C. Do not freeze. Keep the 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

Discard the needle after each injection

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novo Nordisk A/S
Novo Allé
DK-2880 Bagsværd
Denmark

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1160/006 10 pens of 3 mL

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Fiasp

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:

SN:
NN:

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (Cartridge (Penfill))

1. NAME OF THE MEDICINAL PRODUCT

Fiasp 100 units/mL solution for injection in cartridge
insulin aspart

2. STATEMENT OF ACTIVE SUBSTANCE

One cartridge contains 300 units of insulin aspart in 3 mL solution
1 mL solution contains 100 units of insulin aspart (equivalent to 3.5 mg)

3. LIST OF EXCIPIENTS

phenol, metacresol, glycerol, zinc acetate, disodium phosphate dihydrate, arginine hydrochloride, nicotinamide (vitamin B₃), hydrochloric acid/sodium hydroxide (for pH adjustment) and water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
Penfill

5 x 3 mL
10 x 3 mL

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use
Subcutaneous or intravenous use
Designed to be used with Novo Nordisk insulin delivery systems

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 WARNINGS, IF NECESSARY

Use only clear, colourless solution
Single patient use only

8. EXPIRY DATE

EXP

During use: Use within 4 weeks

9. SPECIAL STORAGE CONDITIONS

Before opening: Store in a refrigerator. Do not freeze

During use: Do not refrigerate. Store below 30°C. Do not freeze. Keep the cartridge in the outer carton in order to protect from light

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

Discard the needle after each injection

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novo Nordisk A/S
Novo Allé
DK-2880 Bagsværd
Denmark

12. MARKETING AUTHORISATION NUMBERS

EU/1/16/1160/010 5 cartridges of 3 mL

EU/1/16/1160/011 10 cartridges of 3 mL

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Fiasp

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 (Penfill))

1. NAME OF THE MEDICINAL PRODUCT AND ROUTES OF ADMINISTRATION

Fiasp 100 units/mL solution for injection
insulin aspart
SC, IV

2. METHOD OF ADMINISTRATION

Penfill

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Batch

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3 mL

6. OTHER

Novo Nordisk A/S

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (VIAL)

1. NAME OF THE MEDICINAL PRODUCT

Fiasp 100 units/mL solution for injection in vial
insulin aspart

2. STATEMENT OF ACTIVE SUBSTANCE

One vial contains 1,000 units of insulin aspart in 10 mL solution
1 mL solution contains 100 units of insulin aspart (equivalent to 3.5 mg)

3. LIST OF EXCIPIENTS

phenol, metacresol, glycerol, zinc acetate, disodium phosphate dihydrate, arginine hydrochloride, nicotinamide (vitamin B₃), hydrochloric acid/sodium hydroxide (for pH adjustment) and water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 x 10 mL

5 x 10 mL

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use
Subcutaneous or intravenous use

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

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING, IF NECESSARY

Use only clear, colourless solution

8. EXPIRY DATE

EXP

During use: Use within 4 weeks

9. SPECIAL STORAGE CONDITIONS

Before opening: Store in a refrigerator. Do not freeze

During use: Can be stored in the refrigerator. Store below 30°C. Do not freeze. Keep the vial in the outer carton in order to protect from light.

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

Discard the needle after each injection

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novo Nordisk A/S
Novo Allé
DK-2880 Bagsværd
Denmark

12. MARKETING AUTHORISATION NUMBERS

EU/1/16/1160/007 1 vial of 10 mL
EU/1/16/1160/008 5 vials of 10 mL

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

Fiasp

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 (VIAL)

1. NAME OF THE MEDICINAL PRODUCT AND ROUTES OF ADMINISTRATION

Fiasp 100 units/mL solution for injection
insulin aspart
SC, IV

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Batch

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

10 mL

6. OTHER

Novo Nordisk A/S

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER WRAPPER LABEL ON MULTIPACKS (VIAL – with blue box)

1. NAME OF THE MEDICINAL PRODUCT

Fiasp 100 units/mL solution for injection
insulin aspart

2. STATEMENT OF ACTIVE SUBSTANCE

One vial contains 1,000 units of insulin aspart in 10 mL solution
1 mL solution contains 100 units of insulin aspart (equivalent to 3.5 mg)

3. LIST OF EXCIPIENTS

phenol, metacresol, glycerol, zinc acetate, disodium phosphate dihydrate, arginine hydrochloride, nicotinamide (vitamin B₃), hydrochloric acid/sodium hydroxide (for pH adjustment) and water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

Multipack: 5 (5 packs of 1 x 10 mL)

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use
Subcutaneous or intravenous use

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

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING, IF NECESSARY

Use only clear, colourless solution

8. EXPIRY DATE

EXP
During use: Use within 4 weeks

9. SPECIAL STORAGE CONDITIONS

Before opening: Store in a refrigerator. Do not freeze

During use: Can be stored in the refrigerator. Store below 30°C. Do not freeze. Keep the vial in the outer carton in order to protect from light.

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

Discard the needle after each injection

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novo Nordisk A/S
Novo Allé
DK-2880 Bagsværd
Denmark

12. MARKETING AUTHORISATION NUMBER

EU/1/16/1160/009 5 vials of 10 mL

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Fiasp

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:
SN:
NN:

PARTICULARS TO APPEAR ON THE INNER PACKAGING

CARTON FOR MULTIPACK (VIAL - without blue box)

1. NAME OF THE MEDICINAL PRODUCT

Fiasp 100 units/mL solution for injection in vial
insulin aspart

2. STATEMENT OF ACTIVE SUBSTANCE

One vial contains 1,000 units of insulin aspart in 10 mL solution
1 mL solution contains 100 units of insulin aspart (equivalent to 3.5 mg)

3. LIST OF EXCIPIENTS

phenol, metacresol, glycerol, zinc acetate, disodium phosphate dihydrate, arginine hydrochloride, nicotinamide (vitamin B₃), hydrochloric acid/sodium hydroxide (for pH adjustment) and water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 x 10 mL.
Component of a multipack, cannot be sold separately

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use
Subcutaneous or intravenous use

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

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING, IF NECESSARY

Use only clear, colourless solution

8. EXPIRY DATE

EXP
During use: Use within 4 weeks

9. SPECIAL STORAGE CONDITIONS

Before opening: Store in a refrigerator. Do not freeze

During use: Can be stored in the refrigerator. Store below 30°C. Do not freeze. Keep the vial in the outer carton in order to protect from light.

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

Discard the needle after each injection

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novo Nordisk A/S
Novo Allé
DK-2880 Bagsværd
Denmark

12. MARKETING AUTHORISATION NUMBER

EU/1/16/1160/009 5 vials of 10 mL

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

Fiasp

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:
SN:
NN:

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Fiasp 100 units/mL solution for injection in pre-filled pen insulin aspart

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

What is in this leaflet

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

1. What Fiasp is and what it is used for

Fiasp is a mealtime insulin with a fast-acting blood sugar lowering effect. Fiasp is a solution for injection containing insulin aspart and is used to treat diabetes mellitus in adults. Diabetes is a disease where your body does not produce enough insulin to control the level of blood sugar. Treatment with Fiasp helps to prevent complications from your diabetes.

Fiasp should be injected up to 2 minutes before the start of the meal, with an option to inject up to 20 minutes after starting the meal.

This medicine has its maximum effect between 1 and 3 hours after the injection and the effect lasts for 3 to 5 hours.

This medicine should normally be used in combination with intermediate-acting or long-acting insulin preparations.

This medicine can also be used for continuous infusion in a pump system.

2. What you need to know before you use Fiasp

Do not use Fiasp

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

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Fiasp. Be especially aware of the following:

- Low blood sugar (hypoglycaemia) - If your blood sugar is too low, follow the guidance for low blood sugar in section 4 'Possible side effects'. Fiasp starts to lower blood sugar faster

compared to other mealtime insulins. If hypoglycaemia occurs, you may experience it earlier after an injection with Fiasp.

- High blood sugar (hyperglycaemia) - If your blood sugar is too high, follow the guidance for high blood sugar in section 4 'Possible side effects'.
- Switching from other insulin medicinal products - The insulin dose may need to be changed if you switch from another insulin.
- Pioglitazone used together with insulin - This may increase the risk of heart failure, see under 'Other medicines and Fiasp' below.
- Eye disorder - Fast improvements in blood sugar control may lead to a temporary worsening of diabetic eye disorder.
- Pain due to nerve damage - If your blood sugar level improves very fast, you may get nerve related pain, this is usually temporary.
- Swelling around your joints - When you first start using your medicine, your body may keep more water than it should. This causes swelling around your ankles and other joints. This is usually only short-lasting.

If you have poor eyesight, please see section 3 'How to use Fiasp'.

Some conditions and activities can affect how much insulin you need. Talk to 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 talk to your doctor.

Children and adolescents

This medicine should not be used in children or adolescents, since there is no experience with this medicine in children and adolescents under 18 years of age.

Other medicines and Fiasp

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. Some medicines affect your blood sugar level - this may mean 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 diabetes (oral and injectable)
- sulphonamides - for infections
- anabolic steroids - such as testosterone
- beta-blockers - for e.g., high blood pressure or angina. They may make it harder to recognise the warning signs of low blood sugar (see section 4 'Warning signs of low blood sugar')
- acetylsalicylic acid (and other salicylates) - for pain and mild fever
- monoamine oxidase (MAO) inhibitors - for depression
- angiotensin converting enzyme (ACE) inhibitors - for some heart problems or high blood pressure.

Your blood sugar level may rise (hyperglycaemia) if you take:

- danazol - for endometriosis
- oral contraceptives (birth control pills)
- thyroid hormones - for thyroid problems
- growth hormone - for growth hormone deficiency
- glucocorticoids such as 'cortisone' - for inflammation
- sympathomimetics such as epinephrine (adrenaline), salbutamol or terbutaline - for asthma
- thiazides - for high blood pressure or if your body is keeping too much water (water retention).

Octreotide and lanreotide - used to treat a rare condition involving too much growth hormone (acromegaly). They may increase or decrease your blood sugar level.

Pioglitazone - oral anti-diabetic medicine used to treat type 2 diabetes. Some patients with long-standing type 2 diabetes and heart disease or previous stroke who were treated with pioglitazone and insulin developed heart failure. Tell your doctor immediately if you have signs of heart failure such as unusual shortness of breath, rapid increase in weight or localised swelling (oedema).

If any of the above applies to you (or you are not sure), talk to your doctor or pharmacist.

Fiasp with alcohol

If you drink alcohol, your need for insulin may change as your blood sugar level may either rise or fall. You should therefore monitor your blood sugar level more often than usual.

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. Your insulin dose may need to be changed during pregnancy and after delivery. Careful control of your diabetes is needed in pregnancy. Avoiding low blood sugar (hypoglycaemia) is particularly important for the health of your baby.

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

Driving and using machines

Having low blood sugar can affect your ability to drive or use any tools or machines. If your blood sugar is low, your ability to concentrate or react might be affected. This could be dangerous to yourself or others. Ask your doctor whether you can drive if:

- you often get low blood sugar
- you find it hard to recognise low blood sugar.

Important information about some of the ingredients of Fiasp

This medicine contains less than 1 mmol sodium (23 mg) per dose. This means that this medicine is essentially 'sodium-free'.

3. How to use Fiasp

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

If you are blind or have poor eyesight and cannot read the dose counter on the pen, do not use this pen without help. Get help from a person with good eyesight who is trained to use the FlexTouch pre-filled pen.

The pre-filled pen can provide a dose of 1–80 units in one injection in steps of 1 unit.

When to use Fiasp

Fiasp is a mealtime insulin.

Fiasp should be injected up to 2 minutes before the start of the meal, with an option to inject up to 20 minutes after starting the meal.

This medicine has its maximum effect between 1 and 3 hours after the injection and the effect lasts for 3 to 5 hours.

Fiasp dose

Dose for type 1 and type 2 diabetes

Your doctor will decide together with you:

- how much Fiasp you will need at each meal
- when to check your blood sugar level and if you need a higher or lower dose.

If you want to change your usual diet, check with your doctor, pharmacist or nurse first as a change in diet may alter your need for insulin.

When using other medicines, ask your doctor if your treatment needs to be adjusted.

Dose adjustment for type 2 diabetes

The daily dose should be based on your blood sugar level at mealtimes and bedtime from the previous day.

- Before breakfast - dose should be adjusted according to the blood sugar level before lunch the previous day.
- Before lunch - dose should be adjusted according to the blood sugar level before dinner the previous day.
- Before dinner - dose should be adjusted according to the bedtime blood sugar level the previous day.

Table 1 Dose adjustment		
Mealtime or bedtime blood sugar		Dose adjustment
mmol/L	mg/dL	
less than 4.0	less than 71	Reduce dose by 1 unit
4.0–6.0	71–108	No dose adjustment
more than 6.0	more than 108	Increase dose by 1 unit

Use in elderly patients (65 years or older)

This medicine can be used in elderly patients. Talk to your doctor about changes in your dose.

If you have kidney or liver problems

If you have kidney or liver problems you may need to check your blood sugar level more often. Talk to your doctor about changes in your dose.

Injecting Fiasp

This medicine is for injection under the skin (subcutaneous injection).

Before you use Fiasp for the first time, your doctor or nurse will show you how to use the pre-filled pen.

Where to inject

- The best places to inject are the front of your waist (abdomen) or upper arms.
- Do not inject into a vein or muscle.
- Change the place within the area where you inject each day to reduce the risk of developing changes under the skin (see section 4).

Do not use Fiasp

- if the pen is damaged or if it has not been stored correctly (see section 5 ‘How to store Fiasp’).
- if the insulin does not appear clear (e.g., cloudy) and colourless.

Detailed instructions for use are provided on the other side of this leaflet.

If you use more Fiasp than you should

If you use too much insulin your blood sugar may get too low (hypoglycaemia), see advice in section 4 under ‘Low blood sugar’.

If you forget to use Fiasp

If you forget to use your insulin your blood sugar may get too high (hyperglycaemia). See section 4 under ‘High blood sugar’.

Three simple steps to avoid low or high blood sugar are:

- Always keep a spare pen in case you lose your pen or it gets damaged.

- Always carry something to show you have diabetes.
- Always carry products containing sugar with you. See section 4 under ‘What to do if you get low blood sugar’.

If you stop using Fiasp

Do not stop using your insulin without speaking to your doctor. If you stop using your insulin this could lead to a very high blood sugar level (severe hyperglycaemia) and ketoacidosis (a condition with too much acid in the blood which is potentially life threatening). See symptoms and advice in section 4 under ‘High blood sugar’.

4. Possible side effects

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

Low blood sugar (hypoglycaemia) is very common with insulin treatment (may affect more than 1 in 10 people). It can be very serious. If your blood sugar level falls too much you may become unconscious. Serious hypoglycaemia may cause brain damage and may be life-threatening. If you have symptoms of low blood sugar, take actions **immediately** to increase your blood sugar level. See advice in ‘Low blood sugar’ below.

If you have a serious allergic reaction to insulin or any of the ingredients in Fiasp, stop using this medicine and contact emergency medical service straight away.

Signs of a serious allergic reaction may include:

- local reactions (e.g., rash, redness and itching) spread to other parts of your body
- you suddenly feel unwell with sweating
- you start being sick (vomiting)
- you experience difficulty in breathing
- you experience rapid heartbeat or feeling dizzy.

Allergic reactions such as generalised skin rash and facial swelling may occur. These are uncommon and may affect up to 1 in 100 people. See a doctor if the symptoms worsen or you see no improvement in a few weeks.

Other side effects include:

Common (*may affect up to 1 in 10 people*)

Reaction at administration site: Local reactions at the place you inject yourself may occur. The signs may include: rash, redness, inflammation, bruising and itching. The reactions usually disappear after a few days.

Skin reactions: Signs of allergy on the skin such as eczema, rash, itching, hives and dermatitis may occur.

Uncommon (*may affect up to 1 in 100 people*)

Changes under the skin where you use the injection (lipodystrophy): Fatty tissue under the skin may shrink (lipoatrophy) or get thicker (lipohypertrophy). Changing where you inject each time may reduce the risk of developing these skin changes. If you notice these skin changes, tell your doctor or nurse. If you keep injecting in the same place, these reactions can become more severe and affect the amount of medicine your body gets.

General effects from insulin treatment including Fiasp

- **Low blood sugar (hypoglycaemia)** (very common)

Low blood sugar may happen if you:

Drink alcohol; use too much insulin; exercise more than usual; eat too little or miss a meal.

Warning signs of low blood sugar – these may come on suddenly:

- Headache
- slurred speech
- fast heartbeat
- cold sweat
- cool pale skin
- feeling sick
- feeling very hungry
- tremor or feeling nervous or worried
- feeling unusually tired, weak and sleepy
- feeling confused
- difficulty in concentrating
- short-lasting changes in your sight.

What to do if you get low blood sugar

- If you are conscious, treat your low blood sugar immediately with 15–20 g of fast-acting carbohydrate: eat glucose tablets or another high sugar snack, like fruit juice, sweets or biscuits (always carry glucose tablets or a high sugar snack, just in case).
- It is recommended that you retest your blood glucose levels after 15–20 minutes and re-treat if your blood glucose levels are still less than 4 mmol/L.
- Wait until the signs of low blood sugar have gone or when your blood sugar level has settled. Then carry on with your insulin treatment as usual.

What others need to do if you pass out

Tell everyone you spend time with that you have diabetes. Tell them what could happen if your blood sugar gets too low, including the risk of passing out.

Let them know that if you pass out, they must:

- turn you on your side to avoid choking
- get medical help straight away
- **not** give you any food or drink because you may choke.

You may recover more quickly from passing out with an injection of glucagon. This can only be given by someone who knows how to use it.

- If you are given glucagon you will need sugar or a sugary snack as soon as you come round.
- If you do not respond to a glucagon injection, you will have to be treated in a hospital.

If severe low blood sugar is not treated over time, it can cause brain damage. This can be short or long-lasting. It may even cause death.

Talk to your doctor if:

- your blood sugar got so low that you passed out
- you have been given an injection of glucagon
- you have had too low blood sugar a few times recently.

This is because the dosing or timing of your insulin injections, food or exercise may need to be changed.

- **High blood sugar (hyperglycaemia)** frequency not known (cannot be estimated from the available data)

High blood sugar may happen if you:

Eat more or exercise less than usual; drink alcohol; get an infection or a fever; have not used enough insulin; keep using less insulin than you need; forget to use your insulin or stop using insulin.

Warning signs of high blood sugar – these normally appear gradually:

- Flushed

- dry skin
- feeling sleepy or tired
- dry mouth
- fruity (acetone) breath
- urinating more often
- feeling thirsty
- losing your appetite
- feeling or being sick (nausea or vomiting).

These may be signs of a very serious condition called ketoacidosis. This is a build-up of acid in the blood because the body is breaking down fat instead of sugar. If not treated, this could lead to diabetic coma and eventually death.

What to do if you get high blood sugar

- Test your blood sugar level.
- Give a correction dose of insulin if you have been taught how to do this.
- Test your urine for ketones.
- If you have ketones, seek medical help straight away.

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.

5. How to store Fiasp

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 first use:

Store in a refrigerator (2°C-8°C). Do not freeze. Keep away from the freezing element. Keep the cap on the pen in order to protect from light.

After first opening or if carried as a spare: You can carry your pre-filled pen (FlexTouch) with you and keep it at room temperature (not above 30°C) or in a refrigerator (2°C-8°C) for up to 4 weeks. Always keep the cap on the pen when you are not using it in order to protect from light.

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

6. Contents of the pack and other information

What Fiasp contains

- The active substance is insulin aspart. 1 mL solution contains 100 units of insulin aspart. One pre-filled pen contains 300 units of insulin aspart in 3 mL solution.
- The other ingredients are phenol, metacresol, glycerol, zinc acetate, disodium phosphate dihydrate, arginine hydrochloride, nicotinamide (vitamin B₃), hydrochloric acid (for pH adjustment), sodium hydroxide (for pH adjustment) (see end of section 2 under 'Important information about some of the ingredients of Fiasp') and water for injections.

What Fiasp looks like and contents of the pack

Fiasp is presented as a clear, colourless and aqueous solution for injection in pre-filled pen.

Pack sizes of 1, 5 or a multipack with 2 x 5 pre-filled pens of 3 mL. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Novo Nordisk A/S,
Novo Allé,
DK-2880 Bagsværd, Denmark

Now turn over for information on how to use your FlexTouch.

This leaflet was last revised in

Other sources of information

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

Instructions on how to use Fiasp FlexTouch

Please read these instructions carefully before using your FlexTouch pre-filled pen. If you do not follow the instructions carefully, you may get too little or too much insulin, which can lead to high or low blood sugar level.

Do not use the pen without proper training from your doctor or nurse.

Start by checking your pen to **make sure that it contains Fiasp 100 units/mL**, then look at the illustrations below to get to know the different parts of your pen and needle.

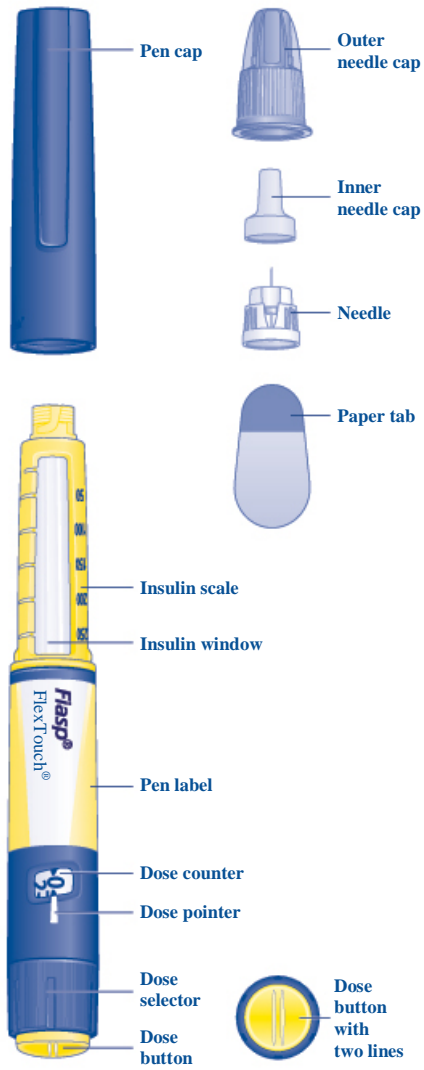
If you are blind or have poor eyesight and cannot read the dose counter on the pen, do not use this pen without help. Get help from a person with good eyesight who is trained to use the FlexTouch pre-filled pen.

Your pen is a pre-filled dial-a-dose insulin pen containing 300 units of insulin. You can select a **maximum of 80 units per dose, in steps of 1 unit**. Your pen is designed to be used with NovoTwist, NovoFine or NovoFine Plus single-use, disposable needles up to a length of 8 mm. Needles are not included in the pack.

Important information

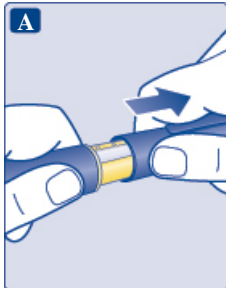
Pay special attention to these notes as they are important for correct use of the pen.

Fiasp pre-filled pen and needle (example) (FlexTouch)

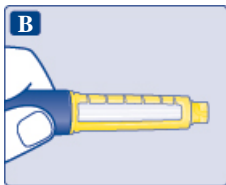


1 Prepare your pen with a new needle

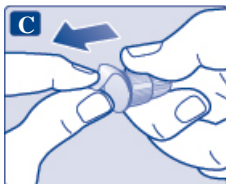
- **Check the name and strength on the label** of your pen, to make sure that it contains Fiasp 100 units/mL. This is especially important if you take more than one type of insulin. If you take a wrong type of insulin, your blood sugar level may get too high or too low.
- **Pull off the pen cap.**



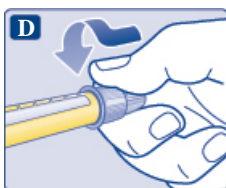
- **Check that the insulin in your pen is clear** and colourless. Look through the insulin window. If the insulin looks cloudy, do not use the pen.



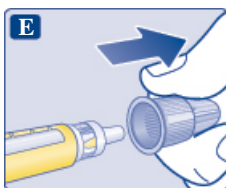
- **Take a new needle** and tear off the paper tab.



- **Push the needle straight onto the pen. Turn until it is on tight.**



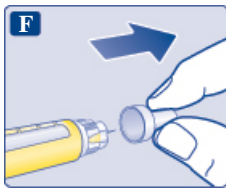
- **Pull off the outer needle cap and keep it for later.** You will need it after the injection, to safely remove the needle from the pen.



- **Pull off the inner needle cap and throw it away.** If you try to put it back on, you may accidentally prick or injure yourself with the needle.

A drop of insulin may appear at the needle tip. This is normal, but you must still check the insulin flow.

Do not attach a new needle to your pen until you are ready for your injection.

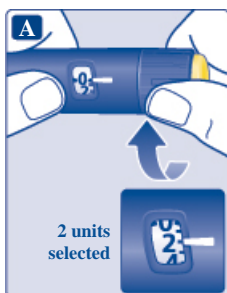


⚠ Always use a new needle for each injection.
This reduces the risk of contamination, infection, leakage of insulin, blocked needles and inaccurate dosing.

⚠ Never use a bent or damaged needle.

2 Check the insulin flow

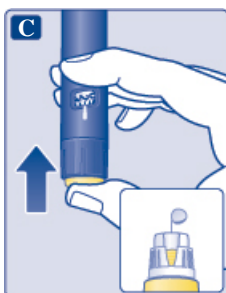
- **Always check the insulin flow before you start.**
This helps you to ensure that you get your full insulin dose.
- Turn the dose selector to **select 2 units. Make sure the dose counter shows 2.**



- Hold the pen with the needle pointing up.
Tap the top of the pen gently a few times to let any air bubbles rise to the top.



- **Press and hold in the dose button** until the dose counter returns to 0.
The 0 must line up with the dose pointer.
A drop of insulin should appear at the needle tip.



A small air bubble may remain at the needle tip, but it will not be injected.

If no drop appears, repeat steps 2A to 2C up to 6 times. If there is still no drop, change the needle and repeat steps 2A to 2C once more.

If a drop of insulin still does not appear, dispose of the pen and use a new one.

! **Always make sure that a drop appears** at the needle tip before you inject. This makes sure that the insulin is flowing properly.

If no drop appears, no insulin will be injected, even though the dose counter may move. This may indicate a blocked or damaged needle.

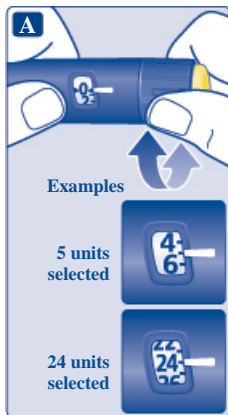
! **Always check the flow before you inject.** If you do not check the flow, you may get too little insulin or no insulin at all. This may lead to high blood sugar level.

3 Select your dose

- **Make sure the dose counter shows 0 before you start.**
The 0 must line up with the dose pointer.
- **Turn the dose selector to select the dose you need**, as directed by your doctor or nurse.

If you select a wrong dose, you can turn the dose selector forwards or backwards to the correct dose.

The pen can dial up to a maximum of 80 units.



The dose selector changes the number of units. Only the dose counter and dose pointer will show how many units you select per dose.

You can select up to 80 units per dose. When your pen contains less than 80 units, the dose counter stops at the number of units left.

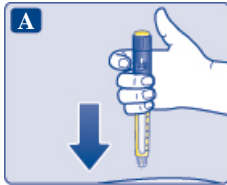
! **Always use the dose counter and the dose pointer to see how many units you have selected before injecting the insulin.**

Do **not** count the pen clicks to set the dose. If you select and inject the wrong dose, your blood sugar level may get too high or too low.

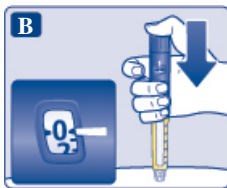
Do not use the insulin scale, it only shows approximately how much insulin is left in your pen. The dose selector clicks differently when turned forwards, backwards or past the number of units left.

4 Inject your dose

- **Insert the needle into your skin** as your doctor or nurse has shown you.
- **Make sure you can see the dose counter.**
Do not touch the dose counter with your fingers. This could interrupt the injection.



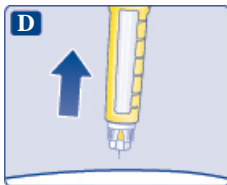
- **Press and hold down the dose button until the dose counter shows 0.**
The 0 must line up with the dose pointer. You may then hear or feel a click.



- **Keep the needle in your skin after** the dose counter has returned to 0 and **count slowly to 6.**
- If the needle is removed earlier, you may see a stream of insulin coming from the needle tip. If so, the full dose will not be delivered, and you should increase the frequency of checking your blood sugar level.



- **Remove the needle from your skin.** If blood appears at the injection site, press lightly on the skin for a few minutes to stop the bleeding. Do not rub the area.



You may see a drop of insulin at the needle tip after injecting. This is normal and does not affect your dose.

- ⚠ **Always watch the dose counter to know how many units you inject.** Hold the dose button down until the dose counter shows 0. If the dose counter does not return to 0, the full dose has not been delivered, which may lead to high blood sugar level.

How to identify a blocked or damaged needle?

- If 0 does not appear in the dose counter after continuously pressing the dose button, you may have used a blocked or damaged needle.

- In this case - you have **not** received **any** medicine - even though the dose counter has moved from the original dose that you have set.

How to handle a blocked needle?

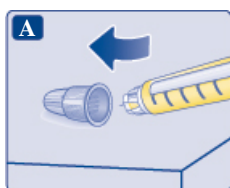
Remove the needle as described in section 5 and repeat all steps starting with section 1: Prepare your pen with a new needle. Make sure you select the full dose you need.

Never touch the dose counter when you inject.

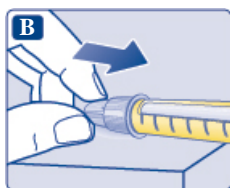
This can interrupt the injection.

5 After your injection

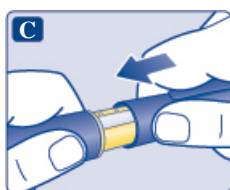
- **Lead the needle tip into the outer needle cap** on a flat surface without touching the needle or the outer cap.



- Once the needle is covered, **carefully push the outer needle cap completely on.**
- **Unscrew the needle** and dispose of it as instructed by your doctor, nurse, pharmacist or local authorities.



- **Put the pen cap on** your pen after each use to protect the insulin from light.



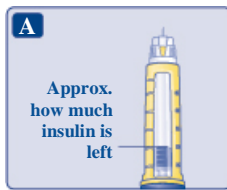
Always dispose of the needle after each injection. This reduces the risk of contamination, infection, leakage of insulin, blocked needles and inaccurate dosing. If the needle is blocked, you will **not** inject any insulin.

When the pen is empty, throw it away **without** a needle on as instructed by your doctor, nurse, pharmacist or local authorities.

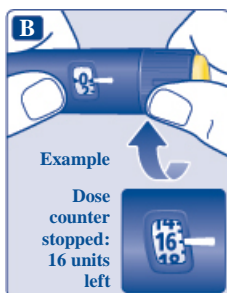
- ⚠ **Never try to put the inner needle cap back on the needle.** You may prick or injure yourself with the needle.
- ⚠ **Always remove the needle from your pen after each injection** and store your pen without the needle attached. This reduces the risk of contamination, infection, leakage of insulin, blocked needles and inaccurate dosing.

6 How much insulin is left?

- The **insulin scale** shows you **approximately** how much insulin is left in your pen.



- **To see precisely how much insulin is left**, use the dose counter:
Turn the dose selector until the **dose counter stops**.
If it shows 80, **at least 80** units are left in your pen.
If it shows **less than 80**, the number shown is the number of units left in your pen.



- Turn the dose selector back until the dose counter shows 0.
 - If you need more insulin than the units left in your pen, you can split your dose between two pens.
- ⚠ Be very careful to calculate correctly if splitting your dose.**
If in doubt, take the full dose with a new pen. If you split the dose wrong, you will inject too little or too much insulin, which can lead to high or low blood sugar levels.

⚠ Further important information

- **Always keep your pen with you.**
- **Always carry an extra pen and new needles** with you, in case of loss or damage.
- Always keep your pen and needles **out of sight and reach of others**, especially children.
- **Never share** your pen or your needles with other people. It might lead to cross-infection.
- **Never share** your pen with other people. Your medicine might be harmful to them.
- Caregivers must **be very careful when handling used needles** – to reduce the risk of needle injury and cross-infection.

Caring for your pen

- Treat your pen with care. Rough handling or misuse may cause inaccurate dosing, which can lead to high or low blood sugar levels.
- **Do not leave the pen in a car** or other place where it can get too hot or too cold.

- **Do not expose your pen to dust, dirt or liquid.**
- **Do not wash, soak or lubricate your pen.** If necessary, clean it with mild detergent on a moistened cloth.
- **Do not drop your pen** or knock it against hard surfaces.
If you drop it or suspect a problem, attach a new needle and check the insulin flow before you inject.
- **Do not try to refill your pen.** Once empty, it must be disposed of.
- **Do not try to repair your pen** or pull it apart.

Package leaflet: Information for the patient

Fiasp 100 units/mL solution for injection in cartridge insulin aspart

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

What is in this leaflet

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

1. What Fiasp is and what it is used for

Fiasp is a mealtime insulin with a fast-acting blood sugar lowering effect. Fiasp is a solution for injection containing insulin aspart and is used to treat diabetes mellitus in adults. Diabetes is a disease where your body does not produce enough insulin to control the level of blood sugar. Treatment with Fiasp helps to prevent complications from your diabetes.

Fiasp should be injected up to 2 minutes before the start of the meal, with an option to inject up to 20 minutes after starting the meal.

This medicine has its maximum effect between 1 and 3 hours after the injection and the effect lasts for 3 to 5 hours.

This medicine should normally be used in combination with intermediate-acting or long-acting insulin preparations.

This medicine can also be used for continuous infusion in a pump system.

2. What you need to know before you use Fiasp

Do not use Fiasp

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

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Fiasp. Be especially aware of the following:

- Low blood sugar (hypoglycaemia) - If your blood sugar is too low, follow the guidance for low blood sugar in section 4 'Possible side effects'. Fiasp starts to lower blood sugar faster

compared to other mealtime insulins. If hypoglycaemia occurs, you may experience it earlier after an injection with Fiasp.

- High blood sugar (hyperglycaemia) - If your blood sugar is too high, follow the guidance for high blood sugar in section 4 'Possible side effects'.
- Switching from other insulin medicinal products - The insulin dose may need to be changed if you switch from another insulin.
- Pioglitazone used together with insulin - This may increase the risk of heart failure, see under 'Other medicines and Fiasp' below.
- Eye disorder - Fast improvements in blood sugar control may lead to a temporary worsening of diabetic eye disorder.
- Pain due to nerve damage - If your blood sugar level improves very fast, you may get nerve related pain, this is usually temporary.
- Swelling around your joints - When you first start using your medicine, your body may keep more water than it should. This causes swelling around your ankles and other joints. This is usually only short-lasting.

If you have poor eyesight, please see section 3 'How to use Fiasp'.

Some conditions and activities can affect how much insulin you need. Talk to 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 talk to your doctor.

Children and adolescents

This medicine should not be used in children or adolescents, since there is no experience with this medicine in children and adolescents under 18 years of age.

Other medicines and Fiasp

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. Some medicines affect your blood sugar level - this may mean 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 diabetes (oral and injectable)
- sulphonamides - for infections
- anabolic steroids - such as testosterone
- beta-blockers - for e.g., high blood pressure or angina. They may make it harder to recognise the warning signs of low blood sugar (see section 4 'Warning signs of low blood sugar')
- acetylsalicylic acid (and other salicylates) - for pain and mild fever
- monoamine oxidase (MAO) inhibitors - for depression
- angiotensin converting enzyme (ACE) inhibitors - for some heart problems or high blood pressure.

Your blood sugar level may rise (hyperglycaemia) if you take:

- danazol - for endometriosis
- oral contraceptives (birth control pills)
- thyroid hormones - for thyroid problems
- growth hormone - for growth hormone deficiency
- glucocorticoids such as 'cortisone' - for inflammation
- sympathomimetics such as epinephrine (adrenaline), salbutamol or terbutaline - for asthma
- thiazides - for high blood pressure or if your body is keeping too much water (water retention).

Octreotide and lanreotide - used to treat a rare condition involving too much growth hormone (acromegaly). They may increase or decrease your blood sugar level.

Pioglitazone - oral anti-diabetic medicine used to treat type 2 diabetes. Some patients with long-standing type 2 diabetes and heart disease or previous stroke who were treated with pioglitazone and insulin developed heart failure. Tell your doctor immediately if you have signs of heart failure such as unusual shortness of breath, rapid increase in weight or localised swelling (oedema).

If any of the above applies to you (or you are not sure), talk to your doctor or pharmacist.

Fiasp with alcohol

If you drink alcohol, your need for insulin may change as your blood sugar level may either rise or fall. You should therefore monitor your blood sugar level more often than usual.

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. Your insulin dose may need to be changed during pregnancy and after delivery. Careful control of your diabetes is needed in pregnancy. Avoiding low blood sugar (hypoglycaemia) is particularly important for the health of your baby.

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

Driving and using machines

Having low blood sugar can affect your ability to drive or use any tools or machines. If your blood sugar is low, your ability to concentrate or react might be affected. This could be dangerous to yourself or others. Ask your doctor whether you can drive if:

- you often get low blood sugar
- you find it hard to recognise low blood sugar.

Important information about some of the ingredients of Fiasp

This medicine contains less than 1 mmol sodium (23 mg) per dose. This means that this medicine is essentially 'sodium-free'.

3. How to use Fiasp

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

If you are blind or have poor eyesight and cannot read the dose counter on the pen, do not use this insulin medicinal product without any help. Get help from a person with good eyesight who is trained to use the pen.

When to use Fiasp

Fiasp is a mealtime insulin.

Fiasp should be injected up to 2 minutes before the start of the meal, with an option to inject up to 20 minutes after starting the meal.

This medicine has its maximum effect between 1 and 3 hours after the injection and the effect lasts for 3 to 5 hours.

Fiasp dose

Dose for type 1 and type 2 diabetes

Your doctor will decide together with you:

- how much Fiasp you will need at each meal
- when to check your blood sugar level and if you need a higher or lower dose.

If you want to change your usual diet, check with your doctor, pharmacist or nurse first as a change in diet may alter your need for insulin.

When using other medicines, ask your doctor if your treatment needs to be adjusted.

Dose adjustment for type 2 diabetes

The daily dose should be based on your blood sugar level at mealtimes and bedtime from the previous day.

- Before breakfast - dose should be adjusted according to the blood sugar level before lunch the previous day.
- Before lunch - dose should be adjusted according to the blood sugar level before dinner the previous day.
- Before dinner - dose should be adjusted according to the bedtime blood sugar level the previous day.

Table 1 Dose adjustment		
Mealtime or bedtime blood sugar		Dose adjustment
mmol/L	mg/dL	
less than 4.0	less than 71	Reduce dose by 1 unit
4.0–6.0	71–108	No dose adjustment
more than 6.0	more than 108	Increase dose by 1 unit

Use in elderly patients (65 years or older)

This medicine can be used in elderly patients. Talk to your doctor about changes in your dose.

If you have kidney or liver problems

If you have kidney or liver problems you may need to check your blood sugar level more often. Talk to your doctor about changes in your dose.

Injecting Fiasp

This medicine is for injection under the skin (subcutaneous injection).

Before you use Fiasp for the first time, your doctor or nurse will show you how to use it.

Where to inject

- The best places to inject are the front of your waist (abdomen) or upper arms.
- Do not inject into a vein or muscle.
- Change the place within the area where you inject each day to reduce the risk of developing changes under the skin (see section 4).

Do not use Fiasp

- if the cartridge or the delivery system you are using is damaged. Take it back to your supplier. See your delivery system manual for further instructions.
- if the cartridge has not been stored correctly (see section 5 'How to store Fiasp').
- if the insulin does not appear clear (e.g., cloudy) and colourless.

How to inject Fiasp

- Read the manual that comes with your insulin delivery system.
- Check the name and strength on the label of the cartridge (Penfill) to make sure it is Fiasp.
- Always use a new needle for each injection to prevent contamination.
- Needles must not be shared.

If you use more Fiasp than you should

If you use too much insulin your blood sugar may get too low (hypoglycaemia), see advice in section 4 under 'Low blood sugar'.

If you forget to use Fiasp

If you forget to use your insulin your blood sugar may get too high (hyperglycaemia). See section 4 under 'High blood sugar'.

Three simple steps to avoid low or high blood sugar are:

- Always keep spare cartridges of Fiasp.
- Always carry something to show you have diabetes.
- Always carry products containing sugar with you. See section 4 under 'What to do if you get low blood sugar'.

If you stop using Fiasp

Do not stop using your insulin without speaking to your doctor. If you stop using your insulin this could lead to a very high blood sugar level (severe hyperglycaemia) and ketoacidosis (a condition with too much acid in the blood which is potentially life threatening). See symptoms and advice in section 4 under 'High blood sugar'.

4. Possible side effects

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

Low blood sugar (hypoglycaemia) is very common with insulin treatment (may affect more than 1 in 10 people). It can be very serious. If your blood sugar level falls too much you may become unconscious. Serious hypoglycaemia may cause brain damage and may be life-threatening. If you have symptoms of low blood sugar, take actions **immediately** to increase your blood sugar level. See advice in 'Low blood sugar' below.

If you have a serious allergic reaction to insulin or any of the ingredients in Fiasp, stop using this medicine and contact emergency medical service straight away.

Signs of a serious allergic reaction may include:

- local reactions (e.g., rash, redness and itching) spread to other parts of your body
- you suddenly feel unwell with sweating
- you start being sick (vomiting)
- you experience difficulty in breathing
- you experience rapid heartbeat or feeling dizzy.

Allergic reactions such as generalised skin rash and facial swelling may occur. These are uncommon and may affect up to 1 in 100 people. See a doctor if the symptoms worsen or you see no improvement in a few weeks.

Other side effects include:

Common (*may affect up to 1 in 10 people*)

Reaction at administration site: Local reactions at the place you inject yourself may occur. The signs may include: rash, redness, inflammation, bruising and itching. The reactions usually disappear after a few days.

Skin reactions: Signs of allergy on the skin such as eczema, rash, itching, hives and dermatitis may occur.

Uncommon (*may affect up to 1 in 100 people*)

Changes under the skin where you use the injection (lipodystrophy): Fatty tissue under the skin may shrink (lipoatrophy) or get thicker (lipohypertrophy). Changing where you inject each time may reduce the risk of developing these skin changes. If you notice these skin changes, tell your doctor or nurse. If you keep injecting in the same place, these reactions can become more severe and affect the amount of medicine your body gets.

General effects from insulin treatment including Fiasp

- **Low blood sugar (hypoglycaemia)** (very common)

Low blood sugar may happen if you:

Drink alcohol; use too much insulin; exercise more than usual; eat too little or miss a meal.

Warning signs of low blood sugar – these may come on suddenly:

- Headache
- slurred speech
- fast heartbeat
- cold sweat
- cool pale skin
- feeling sick
- feeling very hungry
- tremor or feeling nervous or worried
- feeling unusually tired, weak and sleepy
- feeling confused
- difficulty in concentrating
- short-lasting changes in your sight.

What to do if you get low blood sugar

- If you are conscious, treat your low blood sugar immediately with 15–20 g of fast-acting carbohydrate: eat glucose tablets or another high sugar snack, like fruit juice, sweets or biscuits (always carry glucose tablets or a high sugar snack, just in case).
- It is recommended that you retest your blood glucose levels after 15–20 minutes and re-treat if your blood glucose levels are still less than 4 mmol/L.
- Wait until the signs of low blood sugar have gone or when your blood sugar level has settled. Then carry on with your insulin treatment as usual.

What others need to do if you pass out

Tell everyone you spend time with that you have diabetes. Tell them what could happen if your blood sugar gets too low, including the risk of passing out.

Let them know that if you pass out, they must:

- turn you on your side to avoid choking
- get medical help straight away
- **not** give you any food or drink because you may choke.

You may recover more quickly from passing out with an injection of glucagon. This can only be given by someone who knows how to use it.

- If you are given glucagon you will need sugar or a sugary snack as soon as you come round.
- If you do not respond to a glucagon injection, you will have to be treated in a hospital.

If severe low blood sugar is not treated over time, it can cause brain damage. This can be short or long-lasting. It may even cause death.

Talk to your doctor if:

- your blood sugar got so low that you passed out
- you have been given an injection of glucagon
- you have had too low blood sugar a few times recently.

This is because the dosing or timing of your insulin injections, food or exercise may need to be changed.

- **High blood sugar (hyperglycaemia)** frequency not known (cannot be estimated from the available data)

High blood sugar may happen if you:

Eat more or exercise less than usual; drink alcohol; get an infection or a fever; have not used enough insulin; keep using less insulin than you need; forget to use your insulin or stop using insulin.

Warning signs of high blood sugar – these normally appear gradually:

- Flushed
- dry skin
- feeling sleepy or tired
- dry mouth
- fruity (acetone) breath
- urinating more often
- feeling thirsty
- losing your appetite
- feeling or being sick (nausea or vomiting).

These may be signs of a very serious condition called ketoacidosis. This is a build-up of acid in the blood because the body is breaking down fat instead of sugar. If not treated, this could lead to diabetic coma and eventually death.

What to do if you get high blood sugar

- Test your blood sugar level.
- Give a correction dose of insulin if you have been taught how to do this.
- Test your urine for ketones.
- If you have ketones, seek medical help straight away.

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.

5. How to store Fiasp

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 first use:

Store in a refrigerator (2°C-8°C). Do not freeze. Keep away from the freezing element. Keep the cartridge in the carton in order to protect from light.

After first opening or if carried as a spare: Do not refrigerate. You can carry your cartridge (Penfill) with you and keep it at room temperature (not above 30°C) for up to 4 weeks. Always keep the cartridge in the carton in order to protect from light.

Throw away the needle after each injection.

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

6. Contents of the pack and other information

What Fiasp contains

- The active substance is insulin aspart. 1 mL solution contains 100 units of insulin aspart. One cartridge contains 300 units of insulin aspart in 3 mL solution.
- The other ingredients are phenol, metacresol, glycerol, zinc acetate, disodium phosphate dihydrate, arginine hydrochloride, nicotinamide (vitamin B₃), hydrochloric acid (for pH

adjustment), sodium hydroxide (for pH adjustment) (see end of section 2 under ‘Important information about some of the ingredients of Fiasp’) and water for injections.

What Fiasp looks like and contents of the pack

Fiasp is presented as a clear, colourless and aqueous solution for injection in cartridge.

Pack sizes of 5 and 10 cartridges of 3 mL. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Novo Nordisk A/S,
Novo Allé,
DK-2880 Bagsværd, Denmark

This leaflet was last revised in

Other sources of information

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

Package leaflet: Information for the patient

Fiasp 100 units/mL solution for injection in vial insulin aspart

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

What is in this leaflet

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1. What Fiasp is and what it is used for

Fiasp is a mealtime insulin with a fast-acting blood sugar lowering effect. Fiasp is a solution for injection containing insulin aspart and is used to treat diabetes mellitus in adults. Diabetes is a disease where your body does not produce enough insulin to control the level of blood sugar. Treatment with Fiasp helps to prevent complications from your diabetes.

Fiasp should be injected up to 2 minutes before the start of the meal, with an option to inject up to 20 minutes after starting the meal.

This medicine has its maximum effect between 1 and 3 hours after the injection and the effect lasts for 3 to 5 hours.

This medicine should normally be used in combination with intermediate-acting or long-acting insulin preparations.

This medicine can also be used for continuous infusion in a pump system.

2. What you need to know before you use Fiasp

Do not use Fiasp

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

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Fiasp. Be especially aware of the following:

- Low blood sugar (hypoglycaemia) - If your blood sugar is too low, follow the guidance for low blood sugar in section 4 'Possible side effects'. Fiasp starts to lower blood sugar faster

compared to other mealtime insulins. If hypoglycaemia occurs, you may experience it earlier after an injection with Fiasp.

- High blood sugar (hyperglycaemia) - If your blood sugar is too high, follow the guidance for high blood sugar in section 4 'Possible side effects'.
- Switching from other insulin medicinal products - The insulin dose may need to be changed if you switch from another insulin.
- Pioglitazone used together with insulin - This may increase the risk of heart failure, see under 'Other medicines and Fiasp' below.
- Eye disorder - Fast improvements in blood sugar control may lead to a temporary worsening of diabetic eye disorder.
- Pain due to nerve damage - If your blood sugar level improves very fast, you may get nerve related pain, this is usually temporary.
- Swelling around your joints - When you first start using your medicine, your body may keep more water than it should. This causes swelling around your ankles and other joints. This is usually only short-lasting.

Some conditions and activities can affect how much insulin you need. Talk to 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 talk to your doctor.

Children and adolescents

This medicine should not be used in children or adolescents, since there is no experience with this medicine in children and adolescents under 18 years of age.

Other medicines and Fiasp

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. Some medicines affect your blood sugar level - this may mean 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 diabetes (oral and injectable)
- sulphonamides - for infections
- anabolic steroids - such as testosterone
- beta-blockers - for e.g., high blood pressure or angina. They may make it harder to recognise the warning signs of low blood sugar (see section 4 'Warning signs of low blood sugar')
- acetylsalicylic acid (and other salicylates) - for pain and mild fever
- monoamine oxidase (MAO) inhibitors - for depression
- angiotensin converting enzyme (ACE) inhibitors - for some heart problems or high blood pressure.

Your blood sugar level may rise (hyperglycaemia) if you take:

- danazol - for endometriosis
- oral contraceptives (birth control pills)
- thyroid hormones - for thyroid problems
- growth hormone - for growth hormone deficiency
- glucocorticoids such as 'cortisone' - for inflammation
- sympathomimetics such as epinephrine (adrenaline), salbutamol or terbutaline - for asthma
- thiazides - for high blood pressure or if your body is keeping too much water (water retention).

Octreotide and lanreotide - used to treat a rare condition involving too much growth hormone (acromegaly). They may increase or decrease your blood sugar level.

Pioglitazone - oral anti-diabetic medicine used to treat type 2 diabetes. Some patients with long-standing type 2 diabetes and heart disease or previous stroke who were treated with pioglitazone and insulin developed heart failure. Tell your doctor immediately if you have signs of heart failure such as unusual shortness of breath, rapid increase in weight or localised swelling (oedema).

If any of the above applies to you (or you are not sure), talk to your doctor or pharmacist.

Fiasp with alcohol

If you drink alcohol, your need for insulin may change as your blood sugar level may either rise or fall. You should therefore monitor your blood sugar level more often than usual.

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. Your insulin dose may need to be changed during pregnancy and after delivery. Careful control of your diabetes is needed in pregnancy. Avoiding low blood sugar (hypoglycaemia) is particularly important for the health of your baby.

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

Driving and using machines

Having low blood sugar can affect your ability to drive or use any tools or machines. If your blood sugar is low, your ability to concentrate or react might be affected. This could be dangerous to yourself or others. Ask your doctor whether you can drive if:

- you often get low blood sugar
- you find it hard to recognise low blood sugar.

Important information about some of the ingredients of Fiasp

This medicine contains less than 1 mmol sodium (23 mg) per dose. This means that this medicine is essentially 'sodium-free'.

3. How to use Fiasp

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

When to use Fiasp

Fiasp is a mealtime insulin.

Fiasp should be injected up to 2 minutes before the start of the meal, with an option to inject up to 20 minutes after starting the meal.

This medicine has its maximum effect between 1 and 3 hours after the injection and the effect lasts for 3 to 5 hours.

Fiasp dose

Dose for type 1 and type 2 diabetes

Your doctor will decide together with you:

- how much Fiasp you will need at each meal
- when to check your blood sugar level and if you need a higher or lower dose.

If you want to change your usual diet, check with your doctor, pharmacist or nurse first as a change in diet may alter your need for insulin.

When using other medicines, ask your doctor if your treatment needs to be adjusted.

Dose adjustment for type 2 diabetes

The daily dose should be based on your blood sugar level at mealtimes and bedtime from the previous day.

- Before breakfast - dose should be adjusted according to the blood sugar level before lunch the previous day.
- Before lunch - dose should be adjusted according to the blood sugar level before dinner the previous day.
- Before dinner - dose should be adjusted according to the bedtime blood sugar level the previous day.

Table 1 Dose adjustment		
Mealtime or bedtime blood sugar		Dose adjustment
mmol/L	mg/dL	
less than 4.0	less than 71	Reduce dose by 1 unit
4.0–6.0	71–108	No dose adjustment
more than 6.0	more than 108	Increase dose by 1 unit

Use in elderly patients (65 years or older)

This medicine can be used in elderly patients. Talk to your doctor about changes in your dose.

If you have kidney or liver problems

If you have kidney or liver problems you may need to check your blood sugar level more often. Talk to your doctor about changes in your dose.

Injecting Fiasp

This medicine is for injection under the skin (subcutaneous injection) or for continuous infusion in pumps. Administration in a pump will require a comprehensive instruction by your healthcare professional.

Where to inject

- The best places to inject are the front of your waist (abdomen) or upper arms.
- Do not inject into a vein or muscle.
- Change the place within the area where you inject each day to reduce the risk of developing changes under the skin (see section 4).

Do not use Fiasp

- if the protective cap on the vial is loose or missing. The vial contains a protective plastic cap in order to obtain a tamper-proof container. If the vial is not in perfect condition when you get it, return the vial to your supplier.
- if the vial has not been stored correctly (see section 5 ‘How to store Fiasp’).
- if the insulin does not appear clear (e.g., cloudy) and colourless.

How to inject Fiasp

Before you use Fiasp for the first time, your doctor or nurse will show you how to use it.

- 1 Check the name and strength on the label of the vial to make sure it is Fiasp.
- 2 Remove the protective cap from the vial.
- 3 Always use a new needle for each injection to prevent contamination. Needles and syringes must not be shared.
- 4 Draw into the syringe the same amount of air as the dose of insulin you are going to inject. Inject the air into the vial.
- 5 Turn the vial and syringe upside down and draw the correct insulin dose into the syringe. Pull the needle out of the vial. Push the air out of the syringe and check that the dose is correct.
- 6 Inject the insulin under the skin. Use the injection technique advised by your doctor or nurse.
- 7 Throw away the needle after each injection.

For use in an infusion pump system

Follow the instructions and recommendations from your doctor regarding the use of Fiasp in a pump. Before using Fiasp in the pump system, you must have received a comprehensive instruction in the use and information about any actions to be taken in case of illness, high or low blood sugar or failure of the pump system.

Filling the pump

- Fiasp should never be diluted or mixed with any other insulin.
- Before inserting the needle, use soap and water to clean your hands and the skin where the needle is inserted to avoid any infection at the infusion site.
- When you fill a new reservoir, do not leave large air bubbles in either the syringe or the tubing.
- Changing of the infusion set (tubing and needle) must be done according to the instructions in the product information supplied with the infusion set.

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

What to do if the pump system fails

You should always have an alternative delivery method for your insulin available for injection under the skin (for example, a pen injector or syringes) in case the pump system fails.

If you use more Fiasp than you should

If you use too much insulin your blood sugar may get too low (hypoglycaemia), see advice in section 4 under 'Low blood sugar'.

If you forget to use Fiasp

If you forget to use your insulin your blood sugar may get too high (hyperglycaemia). See section 4 under 'High blood sugar'.

Three simple steps to avoid low or high blood sugar are:

- Always keep spare syringes and a spare vial of Fiasp.
- Always carry something to show you have diabetes.
- Always carry products containing sugar with you. See section 4 under 'What to do if you get low blood sugar'.

If you stop using Fiasp

Do not stop using your insulin without speaking to your doctor. If you stop using your insulin this could lead to a very high blood sugar level (severe hyperglycaemia) and ketoacidosis (a condition with too much acid in the blood which is potentially life threatening). See symptoms and advice in section 4 under 'High blood sugar'.

4. Possible side effects

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

Low blood sugar (hypoglycaemia) is very common with insulin treatment (may affect more than 1 in 10 people). It can be very serious. If your blood sugar level falls too much you may become unconscious. Serious hypoglycaemia may cause brain damage and may be life-threatening. If you have symptoms of low blood sugar, take actions **immediately** to increase your blood sugar level. See advice in 'Low blood sugar' below.

If you have a serious allergic reaction to insulin or any of the ingredients in Fiasp, stop using this medicine and contact emergency medical service straight away.

Signs of a serious allergic reaction may include:

- local reactions (e.g., rash, redness and itching) spread to other parts of your body
- you suddenly feel unwell with sweating

- you start being sick (vomiting)
- you experience difficulty in breathing
- you experience rapid heartbeat or feeling dizzy.

Allergic reactions such as generalised skin rash and facial swelling may occur. These are uncommon and may affect up to 1 in 100 people. See a doctor if the symptoms worsen or you see no improvement in a few weeks.

Other side effects include:

Common (*may affect up to 1 in 10 people*)

Reaction at administration site: Local reactions at the place you inject yourself may occur. The signs may include: rash, redness, inflammation, bruising and itching. The reactions usually disappear after a few days.

Skin reactions: Signs of allergy on the skin such as eczema, rash, itching, hives and dermatitis may occur.

Uncommon (*may affect up to 1 in 100 people*)

Changes under the skin where you use the injection (lipodystrophy): Fatty tissue under the skin may shrink (lipoatrophy) or get thicker (lipohypertrophy). Changing where you inject each time may reduce the risk of developing these skin changes. If you notice these skin changes, tell your doctor or nurse. If you keep injecting in the same place, these reactions can become more severe and affect the amount of medicine your body gets.

General effects from insulin treatment including Fiasp

- **Low blood sugar (hypoglycaemia)** (very common)

Low blood sugar may happen if you:

Drink alcohol; use too much insulin; exercise more than usual; eat too little or miss a meal.

Warning signs of low blood sugar – these may come on suddenly:

- Headache
- slurred speech
- fast heartbeat
- cold sweat
- cool pale skin
- feeling sick
- feeling very hungry
- tremor or feeling nervous or worried
- feeling unusually tired, weak and sleepy
- feeling confused
- difficulty in concentrating
- short-lasting changes in your sight.

What to do if you get low blood sugar

- If you are conscious, treat your low blood sugar immediately with 15–20 g of fast-acting carbohydrate: eat glucose tablets or another high sugar snack, like fruit juice, sweets or biscuits (always carry glucose tablets or a high sugar snack, just in case).
- It is recommended that you retest your blood glucose levels after 15–20 minutes and re-treat if your blood glucose levels are still less than 4 mmol/L.
- Wait until the signs of low blood sugar have gone or when your blood sugar level has settled. Then carry on with your insulin treatment as usual.

What others need to do if you pass out

Tell everyone you spend time with that you have diabetes. Tell them what could happen if your blood sugar gets too low, including the risk of passing out.

Let them know that if you pass out, they must:

- turn you on your side to avoid choking
- get medical help straight away
- **not** give you any food or drink because you may choke.

You may recover more quickly from passing out with an injection of glucagon. This can only be given by someone who knows how to use it.

- If you are given glucagon you will need sugar or a sugary snack as soon as you come round.
- If you do not respond to a glucagon injection, you will have to be treated in a hospital.

If severe low blood sugar is not treated over time, it can cause brain damage. This can be short or long-lasting. It may even cause death.

Talk to your doctor if:

- your blood sugar got so low that you passed out
- you have been given an injection of glucagon
- you have had too low blood sugar a few times recently.

This is because the dosing or timing of your insulin injections, food or exercise may need to be changed.

- **High blood sugar (hyperglycaemia)** frequency not known (cannot be estimated from the available data)

High blood sugar may happen if you:

Eat more or exercise less than usual; drink alcohol; get an infection or a fever; have not used enough insulin; keep using less insulin than you need; forget to use your insulin or stop using insulin.

Warning signs of high blood sugar – these normally appear gradually:

- Flushed
- dry skin
- feeling sleepy or tired
- dry mouth
- fruity (acetone) breath
- urinating more often
- feeling thirsty
- losing your appetite
- feeling or being sick (nausea or vomiting).

These may be signs of a very serious condition called ketoacidosis. This is a build-up of acid in the blood because the body is breaking down fat instead of sugar. If not treated, this could lead to diabetic coma and eventually death.

What to do if you get high blood sugar

- Test your blood sugar level.
- Give a correction dose of insulin if you have been taught how to do this.
- Test your urine for ketones.
- If you have ketones, seek medical help straight away.

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.

5. How to store Fiasp

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 first use:

Store in a refrigerator (2°C-8°C). Do not freeze. Keep away from the freezing element. Keep the vial in the carton in order to protect from light.

After first opening or if carried as a spare: You can carry your vial with you and keep it at room temperature (not above 30°C) or in a refrigerator (2°C-8°C) for up to 4 weeks. Always keep the vial in the carton 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 Fiasp contains

- The active substance is insulin aspart. 1 mL solution contains 100 units of insulin aspart. One vial contains 1,000 units of insulin aspart in 10 mL solution.
- The other ingredients are phenol, metacresol, glycerol, zinc acetate, disodium phosphate dihydrate, arginine hydrochloride, nicotinamide (vitamin B₃), hydrochloric acid (for pH adjustment), sodium hydroxide (for pH adjustment) (see end of section 2 under 'Important information about some of the ingredients of Fiasp') and water for injections.

What Fiasp looks like and contents of the pack

Fiasp is presented as a clear, colourless and aqueous solution for injection in a vial. Each vial contains 10 mL solution.

Pack sizes of 1, 5 or a multipack with 5 x (1 x 10 mL) vials. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Novo Nordisk A/S,
Novo Allé,
DK-2880 Bagsværd, Denmark

This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency website:

<http://www.ema.europa.eu>.