APPROVED PROFESSIONAL INFORMATION

SCHEDULING STATUS:

S3

1. NAME OF THE MEDICINE

Fiasp

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Contains insulin aspart 100 *U/ml*. One unit of insulin aspart corresponds to 6 nmol; 0,035 *mg* salt-free anhydrous insulin aspart (recombinant DNA origin, *Saccharomyces cerevisiae).*

3. PHARMACEUTICAL FORM

Solution for injection,

A sterile, clear, colourless, aqueous, neutral solution of insulin aspart (B28 Asp), free from visible particulate matter.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Maintenance treatment of diabetes mellitus in adults, adolescents and children aged 1 year and above, used alone or in combination with other insulins or metformin.

4.2 Posology and method of administration

Posology

Dosage

Fiasp® is a mealtime insulin for subcutaneous administration at the start of a meal or post-meal (within 20 minutes after starting a meal).

Fiasp can be used for continuous subcutaneous insulin infusion (CSII) in pumps or be administrated intravenously by healthcare professionals.

The potency of 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.

Dosing with Fiasp® is individual and determined in accordance with the needs of the patient.

Injection therapy:

Fiasp® 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 remainder by intermediate acting or long-acting insulin.

Continuous subcutaneous insulin infusion (CSII):

Fiasp® can be used for continuous subcutaneous insulin infusion (CSII) in pumps. In this case, Fiasp® will cover both the need for bolus insulin (approximately 50 %) and basal insulin.

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

The individual total daily insulin requirement in adults, adolescents and children, may vary and is usually between 0,5 and 1,0 *unit/kg/day.*

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.

Initiation

Patients with type 1 diabetes mellitus

The recommended starting dose of Fiasp® in insulin naïve patients with type 1 diabetes is approximately 50 % of the total daily insulin dose and should be divided between each daily meal. 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.

Transfer from other insulin medicines

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. Due to the fast onset of insulin action, Fiasp® should be injected at the start of a meal or post-meal (within 20 minutes after starting a meal).

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 or long-acting insulin products or other concomitant antidiabetic treatment may need to be adjusted.

Patients with type 2 diabetes mellitus

Fiasp® adjustment may be considered daily based on mealtime and bedtime SMPG (Self Monitoring Plasma Glucose) on the previous day according to Table 1

- Pre-breakfast Fiasp® should be adjusted according to the pre-lunch SMPG (Self Monitoring Plasma Glucose) the previous day
- Pre-lunch Fiasp® should be adjusted according to the pre-dinner SMPG the previous day
- Pre-dinner Fiasp® should be adjusted according to the bedtime SMPG the previous day.

Table 1 **Dose adjustment**	
Mealtime or bedtime plasma glucose SMPG (see above)	Dose adjustment
mmol/l	Unit
< 4,0	-1
4,0 – 6,0	No adjustment
> 6,0	+1

Elderly (≥ 65 years old)

The safety and efficacy of Fiasp® has been established in elderly patients. Close glucose monitoring is recommended and the insulin dose should be adjusted on an individual basis (*see PD, PK* sections and clinical efficacy and safety data).

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 PK section*).

Paediatric population

Fiasp® can be used in adolescents and children aged 1 year and above (*see section 3.1*).

Method of administration

Subcutaneous injection:

Fiasp® is administered subcutaneously by injection in the abdominal wall, the upper arm or the thigh. Injection sites should always be rotated within the same region in order to reduce the risk of lipodystrophy and cutaneous amyloidosis (*see sections 4.2 and 4.3*).

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

Continuous Subcutaneous Insulin Infusion (CSII):

Fiasp® has been used in limited number of patients for Continuous Subcutaneous Insulin Infusion (CSII) in pumps suitable for insulin infusion. Fiasp® can be administered in accordance with the instructions provided by the pump manufacturer, preferably in the abdomen. Infusion sites should be rotated within the same region to reduce the risk of lipodystrophy.

When used with an insulin infusion pump, Fiasp® should not be diluted or mixed with any other insulin medicines.

Patients using CSII should be instructed in the use of the pump and use the correct reservoir and tubing for pump. The infusion set (tubing and cannula) should be changed in accordance with the instructions in the medicine 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 Fiasp® 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 0,9 % sodium chloride or 5 % dextrose.

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.

Substances added to Fiasp® may cause degradation of insulin aspart.
Fiasp® must not be diluted or mixed with any other products except infusion fluids as described in method of administration.

Missed dose
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.

4.3 Contra-indications

- Hypersensitivity to the insulin aspart or any of the excipients listed under *"Composition*".
- During episodes of hypoglycaemia

4.4 Special warnings and precautions for use

The safe use of Fiasp in treatment of ketoacidosis has not been established.

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 "*OVERDOSE"*).

Severe hypoglycaemia may lead to unconsciousness and/or convulsions and may result in temporary or permanent impairment of brain function or even death. The symptoms of hypoglycaemia usually occur suddenly. They may include cold sweats, cool pale skin, fatigue, nervousness or tremor, anxiousness, unusual tiredness or weakness, confusion, difficulty in concentrating, drowsiness, excessive hunger, vision changes, headache, nausea and palpitation.

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

The timing of hypoglycaemia usually reflects the time-action profile of the administered insulin formulation. Fiasp® has a distinct time action profile, which impacts the timing of hypoglycaemia.

A consequence of the pharmacodynamics of Fiasp® is that if hypoglycaemia occurs, it may occur earlier after an injection/infusion when compared to other mealtime insulins. Since Fiasp® should be administered at the start of a meal or postmeal (within 20 minutes after starting a meal), the fast onset of action should therefore be considered in patients with delayed gastric emptying.

Paediatric population

Close monitoring of blood glucose levels is recommended if administering this medicine after the start of the last meal of the day, in order to avoid nocturnal hypoglycaemia.

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.

The first symptoms of hyperglycaemia usually come on gradually, over a period of hours or days. They include nausea, vomiting, drowsiness, flushed dry skin, dry mouth, increased urination, thirst and loss of appetite as well as acetone breath.

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.

Clinical safety data with use of Fiasp by continuous subcutaneous insulin infusion (CSII) in pumps is limited

Concomitant diseases in the kidney, liver or affecting the adrenal, pituitary or thyroid gland may require changes in the insulin dose.

Combination of pioglitazone and insulin medicines

Cases of congestive heart failure have been reported when pioglitazone was 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 pioglitazone and insulin medicines is considered. If the combination is used, patients

should be observed for signs and symptoms of congestive heart failure, weight gain and oedema. Pioglitazone 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. 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 Fiasp® and other insulin medicines.

Patients must visually verify the units of the dose prior to administering Fiasp®. 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.

Allergic reactions

Anaphylactic reactions may occur. Immediate-type allergic reactions to either insulin itself or the excipients may potentially be life-threatening.

Skin and subcutaneous tissue disorders

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

4.5 Interaction with other medicines and other forms of interaction

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

The following substances may reduce insulin requirement:

Oral antidiabetic medicines, monoamine oxidase inhibitors (MAOIs), beta-blockers, angiotensin converting enzyme (ACE) inhibitors, salicylates, anabolic steroids, angiotensin receptor blockers (ARB's), 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 medicines 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 Pregnancy and lactation

Pregnancy

Safety in pregnancy has not been established.

Insulin aspart does not cross the placental barrier. Intensified blood glucose control and monitoring of pregnant women with diabetes (Type 1, Type 2 or gestational diabetes) are recommended throughout pregnancy and when contemplating pregnancy. Both hypoglycaemia and hyperglycaemia which can occur in inadequately controlled diabetes therapy may increase the risk of malformations and death in utero.

Insulin requirements usually fall in the first trimester and increase subsequently during the second and third trimesters. After delivery, insulin requirements return rapidly to pre-pregnancy levels.

Breast-feeding

Safety during breast-feeding has not been established.
There are no restrictions on treatment with Fiasp during breastfeeding as insulin aspart does not cross into breast milk. However, the Fiasp dosage may need to be adjusted.

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 operating machinery).

Patients should be advised to take precautions to avoid hypoglycaemia while driving. This is particularly important in those patients 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

(a) Summary of the safety profile

The most frequently reported side effect during treatment is hypoglycaemia *(see section 'Description of selected side effects* below).

(b) Tabulated summary of adverse reactions

Side effects from clinical trials

Side effects listed below are based on data from 6 completed therapeutic confirmatory trials in adults. In five of the trials Fiasp® was compared to comparator insulin and in one trial compared to basal insulin only. In the six trials, 2163 patients were treated with Fiasp®; 1707 with type 1 diabetes mellitus of which 261 were using CSII, and 456 with type 2 diabetes mellitus.

The side effects are classified according to MedDRA System Organ Class. Frequency categories are defined according to the following convention:
Very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1 000 to < 1/100).

Table 2 Side effects 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	

Other possible side effects

Based on clinical trial data from other insulin aspart products:

System organ class	*Side effect and frequency*
Immune system disorders	*Uncommon*: Eruptions
	Very rare Anaphylactic reactions
Eye disorders	*Uncommon* Refraction (blurred vision)
	Uncommon Diabetic retinopathy:
General disorders and administration site conditions	*Uncommon* Oedema:
Nervous system disorders	*Rare* Peripheral neuropathy (painful neuropathy)

Side effects from post-marketing sources

The side effect listed below is based on post-marketing source data and is classified according to MedDRA System Organ Class.

MEDRA System organ class	*Side effect and frequency*
Skin and subcutaneous tissue disorders	*Frequency: Unknown* Cutaneous amyloidosis

(c) 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. 0,3 % for comparator). Based on post-marketing data, serious forms of systemic allergic reactions may occur.

Immediate-type allergic reactions to either insulin itself or the excipients may potentially be life-threatening.

Skin and subcutaneous tissue disorders

Lipodystrophy (including lipohypertrophy, lipoatrophy) and cutaneous amyloidosis may occur at the injection site and delay local insulin absorption.

Lipodystrophy was reported at the injection/infusion site in patients treated with Fiasp® (0,5 % vs. 0,2 % in comparator). Continuous rotation of the injection site within the given injection area may help to reduce or prevent these reactions (see section 4.3)

Injection/infusion site reactions

Infusion site reactions (including redness, inflammation, irritation, pain, bruising, and itching) were reported in patients treated with Fiasp® (10,0 % vs. 8,3 % in comparator). These reactions are usually mild and transitory and they normally disappear during continued treatment.

Paediatric population

Fiasp® has been administered to children and adolescents from 6 years up to 18 years of age for the investigation of pharmacokinetic properties.

Safety and efficacy have been investigated in a therapeutic confirmatory trial in children with type 1 diabetes mellitus aged 1 to less than 18 years. In the trial, 519 patients were treated with Fiasp®. Overall the frequency, type and severity of adverse reactions in the paediatric population do not indicate differences to the experience in the adult population.

Lipodystrophy (including lipohypertrophy, lipoatrophy) at the injection site was reported more often in paediatric patients compared to adults. In the paediatric population

lipodystrophy was reported with a frequency of 2,1 % for Fiasp® vs. 1,6 % for comparator.

Other special populations

Based on results from clinical trials, the frequency, type and severity of side effects 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. Fiasp® has been administered to elderly patients for the investigation of pharmacokinetic properties.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine 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 "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications *https://www.sahpra.org.za/Publications/Index/8*

4.9 Overdose

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 medicines containing sugar. It is therefore recommended that the diabetic patient always carries glucose-containing medicines.
- Severe hypoglycaemic episodes, where the patient is not able to treat him/herself, can be treated with glucagon (0,5 to 1,0 *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: Medicines used in diabetes, Insulins and analogues for injection, fast-acting, ATC code: A10AB01 (A 21.1 Insulin preparations)

Mechanism of action and pharmacodynamic effects

Insulin aspart, binds 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.

The addition of niacinamide (vitamin B3) results in a fast initial absorption of insulin, leading to an early onset of action and early glucose-lowering effect.

The time course of insulin action may vary considerably in different individuals or within the same individual. The average onset of action for fast-acting insulin aspart is 16 − 20 minutes and time to maximum effect 91 − 133 minutes for subcutaneous administration. The duration of action is 3 to 5 hours depending on dose.

Insulin aspart administered at mealtime reduced estimated mean 1-hour and 2-hour postprandial glucose (PPG) concentrations by -1,0 mmol/l and -0,44 mmol/l, respectively after 26 weeks of randomised treatment.

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

There is no clinically relevant difference in the pharmacodynamic properties of fast acting insulin aspart between children (6 - 11 years), adolescents (12 - 18 years) and adult patients with type 1 diabetes mellitus.

5.2 Pharmacokinetic properties

Absorption

Fast-acting insulin aspart is a mealtime insulin aspart formulation in which the addition of niacinamide (vitamin B3) results in a fast initial absorption of insulin, leading to an early onset of exposure and early insulin exposure following bolus administration via subcutaneous injection (*Figure 1*) or through CSII in pumps.

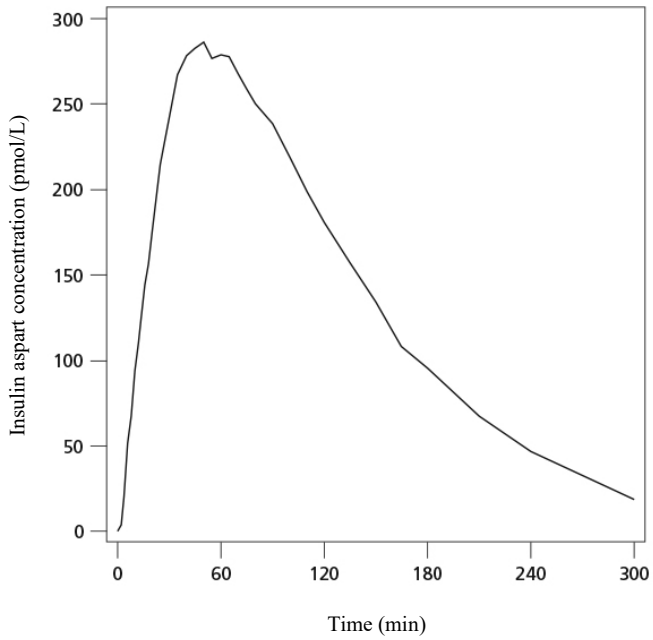


Figure 1 – Mean insulin profile in patients with type 1 diabetes after subcutaneous injection of 0,2 U/kg fast acting insulin aspart

Insulin aspart appeared in the circulation approximately 4 minutes after administration. The average time to maximum insulin concentrations ($t_{max, IAsp}$) was 54 − 68 *minutes* after administration.

The total exposure ($AUC_{0-12\,h,\,IAsp}$) and maximum insulin aspart concentration ($C_{max,\,IAsp}$) increases proportionally with increasing subcutaneous dose of fast-acting insulin aspart within the therapeutic dose range.

Continuous Subcutaneous Insulin Infusion (CSII)

In CSII setting, the average time to reach 50 % maximum insulin concentration ($C_{max,\,IAsp}$) was 21 minutes and time to maximum insulin concentration ($t_{max,\,IAsp}$) was 57 minutes after a bolus administration. Time to late 50 % $C_{max,\,IAsp}$ (a measure of offset) was 137 minutes after bolus administration.

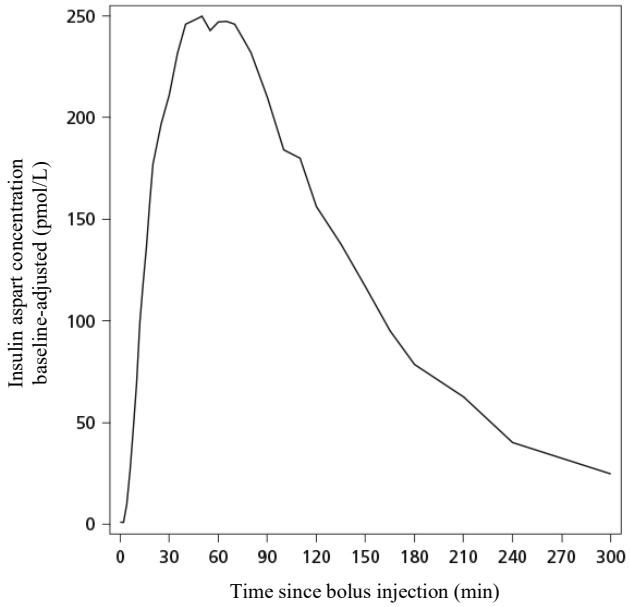


Figure 2: Mean insulin profile in patients with type 1 diabetes in a CSII setting after administration of 0,15 U/kg fast-acting insulin aspart (corrected for basal insulin infusion)

Distribution

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

Biotransformation

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

Elimination

Half-life after subcutaneous administration of insulin aspart is 57 minutes.

Gender

The early and maximum insulin exposure of insulin aspart 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 effect of BMI on the total insulin exposure of insulin aspart was based on results from a population pharmacokinetic analysis in patients with type 1 diabetes. No relationship between total insulin exposure and BMI was observed.

Hepatic impairment

Hepatic impairment may reduce the patient's insulin requirements.

Renal impairment

Renal function was defined using creatinine clearance (CLcr) as follows: ≥ 90 *ml/min* (normal) (N = 546), 60 - 89 *ml/min* (mild) (N = 115), 30 - 59 *ml/min* (moderate) (N = 21). Higher total exposure was observed with decreasing renal function for insulin aspart. However, there was some between subject variability in total exposure across patients with type 1 diabetes with mild or moderate renal impairment. Thus glucose monitoring should be intensified and the insulin aspart dosage adjusted on an individual basis in patients with renal impairment.

Paediatric population

The efficacy and safety of fast acting insulin aspart have been studied in a 1:1:1 randomised active controlled clinical trial in children and adolescents with type 1 diabetes mellitus for a period of 26 weeks (n = 777). In this trial the efficacy and safety of fast acting insulin aspart administered at mealtime (0 – 2 minutes before meal) or post-meal (20 minutes after meal start) and comparator administered at mealtime, both used in combination with insulin degludec, were compared.

Patients in the fast acting insulin aspart mealtime arm included 16 children aged 1 – 5 years, 100 children aged 6 – 11 years and 144 adolescents aged 12 – 17 years. Patients in the fast acting insulin aspart postmeal arm included 16 children aged 1 – 5 years, 100 children aged 6 – 11 years and 143 adolescents aged 12 – 17 years.

Fast acting Insulin aspart was shown to be effective in terms of glycaemic control, both when administered postmeal (ETD: 0,13 % [-0,01; 0,26] 95 % CI) and at mealtime (ETD: -0,17 % [-0,30; -0,03] 95 % CI), compared to comparator

No overall increased risk of severe or blood glucose confirmed hypoglycaemia was observed**.**

The observed effects and the safety profiles were comparable between all age groups.

In children (6 - 11 years) and adolescents (12 - 18 years) fast acting insulin aspart showed, an earlier onset of exposure and a higher early insulin exposure whilst maintaining a similar total exposure and maximum concentration compared to comparator.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Preservatives:

The following preservatives are included: Phenol: 0,15 % m/v (1,50 *mg/ml*) and Metacresol: 0,172 % m/v (1,72 *mg/ml*)

Other excipients

Glycerol

Zinc acetate

Disodium phosphate dihydrate

Arginine hydrochloride

Niacinamide (vitamin B3)

Water for injections

6.2 Incompatibilities

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

6.3 Shelf life

Before opening:

30 months,

Stored in a refrigerator (2 °C – 8 °C).

After first opening or carried as a spare:

4 weeks (28 days).

Stored at or below 30 °C

6.4 Special precautions for storage

Before first use:

Store in a refrigerator (2 °C – 8 °C).

Keep away from the freezing element.

Do not freeze.

FlexTouch®: Keep the cap on the pen in order to protect from light.

Vial/Penfill®**:** Keep the vial/cartridge in the carton in order to protect from light.

After first opening or carried as a spare:

FlexTouch®:

Store at or below 30 °C for not more than 4 weeks (28 days).

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

Vial:

Store at or below 30 °C for not more than 4 weeks (28 days).

Can be stored in the refrigerator (2 °C – 8 °C). Do not freeze.

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

Penfill®:

Do not refrigerate.

Store at or below 30 °C for not more than 4 weeks (28 days)

Do not freeze. If cartridge is carried as a spare and unused, the cartridge should be kept in the carton in order to protect from light.

6.5 Nature and contents of container

FlexTouch®:

3 ml solution in a cartridge (type 1 colourless glass) with a grey plunger (halobutyl) and a cream stopper (halobutyl/polyisoprene) contained in a pre-filled multidose disposable

pen made of polypropylene, polyoxymethylene, polycarbonate and acrylonitrile butadiene styrene.

The pen is blue when capped, with red dose button, on removal of the cap the pen consists of red cartridge holder with blue housing, labelled with red and yellow stripped label.

The pen(s) is/are packed in carton box

Pack sizes of:

- 1 x 3 ml FlexTouch (pre-filled pen)
- 5 X 3 ml FlexTouch (pre-filled pens)
- A multipack with 2 x (5 x 3 ml FlexTouch) pre-filled pens.
- 1 X 3 ml FlexTouch (pre-filled pen) including 7 NovoFine® Plus needles
- 1 X 3 ml FlexTouch (pre-filled pen) including 7 NovoFine® needles
- 1 X 3 ml FlexTouch (pre-filled pen) including 7 NovoTwist® needles

Vial:

10 ml solution in vial (type 1 colourless glass) closed with a halobutyl/polyisoprene cream rubber disc and a protective tamper-proof yellow plastic cap. The vial(s) is/are packed in carton box.

Pack sizes of:

- 1 x 10 ml vial
- 5 x 10 ml vials

A multipack with 5 x (1 x 10 ml) vials.

Penfill®:

3 ml solution in cartridge (type 1 colourless glass), with a grey plunger (halobutyl) and a cream stopper (halobutyl/polyisoprene). The cartridge is packaged in press through

blister pack made of aluminium foil and polyethylene terephthalate (PET). The blister is packed in a carton box.

Pack sizes of:

- 5 x 3 ml Penfill (cartridges)
- 10 x 3 ml Penfill (cartridges)

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Discard any unused portion after 4 weeks (28 days).

Fiasp® exposed to temperatures higher than 37 °C should be discarded.

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

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.

Cartridges, needles and pre-filled pens must not be shared.

The cartridge must not be refilled.

Disposal

Any unused Fiasp injection or waste material should be disposed of in accordance with local requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Novo Nordisk (Pty) Ltd

150 Rivonia Road

10 Marion Street Office Park

Building C1

Sandton, Johannesburg

2196

8. REGISTRATION NUMBERS

51/21.1/0733

9. DATE OF FIRST AUTHORISATION

Date on the registration certificate of the medicine: 09 December 2019

10. DATE OF REVISION OF THE TEXT

Date of the most recently revised Professional Information as approved by SAHPRA:

09 February 2022