insulin aspart injection 100 units/mL

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use FIASP® safely and effectively. See full prescribing information for FIASP®.

FIASP® (insulin aspart injection) for subcutaneous or intravenous use
Initial U.S. Approval: 2000

——— RECENT MAJOR CHANGES ———

Dosage and Administration (2.2, 2.3) ——— 10/2019
Warnings and Precautions (5.2, 5.8) ——— 10/2019

——— INDICATIONS AND USAGE ———

• FIASP® is a rapid-acting human insulin analog indicated to improve glycemic control in adults with diabetes mellitus (1).

——— DOSAGE AND ADMINISTRATION ———

• Individualize and adjust the dosage of FIASP® based on route of administration, individual’s metabolic needs, blood glucose monitoring results and glycemic control goal (2.2).

• Dosage adjustments may be needed when switching from another insulin, with changes in physical activity, changes in concomitant medications, changes in meal patterns, changes in renal or hepatic function or during acute illness (2.2).

• Subcutaneous injection (2.2):
  o Inject at the start of a meal or within 20 minutes after starting a meal into the abdomen, upper arm, or thigh.
  o Rotate injection sites within the same region to reduce the risk of lipodystrophy and localized cutaneous amyloidosis.
  o Should generally be used in regimens with an intermediate- or long-acting insulin.

• Continuous Subcutaneous Infusion (Insulin Pump) (2.2):
  o Refer to the insulin infusion pump user manual to see if FIASP® can be used. Use in accordance with the insulin pumps’ instructions for use.
  o Administer by continuous subcutaneous infusion using an insulin pump in a region recommended in the instructions from the pump manufacturer. Rotate infusion sites within the same region to reduce the risk of lipodystrophy and localized cutaneous amyloidosis.

• Intravenous Infusion: Administer only under medical supervision after diluting to concentrations from 0.5 to 1 unit/mL insulin aspart in infusion systems using polypropylene infusion bags (2.2).

——— DOSAGE FORMS AND STRENGTHS ———

Injection: 100 units/mL (U-100):
• 10 mL multiple-dose vial (3)
• 3 mL single-patient-use FIASP® FlexTouch® pen (3)
• 3 mL single-patient-use PenFill® cartridges for use in a PenFill® cartridge device (3)

——— CONTRAINDICATIONS ———

• Never share a FIASP® FlexTouch® pen, PenFill® cartridge or PenFill® cartridge device between patients, even if the needle is changed (5.1).

• Hypoglycemia or hypoglycemia with changes in insulin regimen: Make changes to a patient’s insulin regimen (e.g., insulin strength, manufacturer, type, injection site or method of administration) under close medical supervision with increased frequency of blood glucose monitoring (5.2).

• Hypoglycemia: May be life-threatening. Increase frequency of glucose monitoring with changes to: insulin dosage, co-administered glucose lowering medications, meal pattern, physical activity, and in patients with renal impairment or hepatic impairment or hypoglycemia unawareness (5.3).

• Hypoglycemia due to medication errors: Accidental mix-ups between insulin products can occur. Instruct patients to check insulin labels before injection (5.4).

• Hypokalemia: May be life-threatening. Monitor potassium levels in patients at risk for hypokalemia and treat if indicated (5.5).

• Hypersensitivity reactions: Severe, life-threatening, generalized allergy, including anaphylaxis, can occur. Discontinue FIASP®, monitor and treat if indicated (5.6).

• Fluid retention and heart failure with concomitant use of thiazolidinediones (TZDs): Observe for signs and symptoms of heart failure; consider dosage reduction or discontinuation if heart failure occurs (5.7).

• Hyperglycemia and Ketonacidosis Due to Insulin Pump Device Malfunction: Monitor glucose and administer FIASP® by subcutaneous injection if pump malfunction occurs (5.8).

——— ADVERSE REACTIONS ———

Adverse reactions observed with FIASP® include: hypoglycemia, allergic reactions, hypersensitivity, injection/infiltration site reactions, lipodystrophy, and weight gain (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact Novo Nordisk Inc. at 1-800-727-6500 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

——— DRUG INTERACTIONS ———

• Drugs that Blunt Hypoglycemia Signs and Symptoms (e.g., beta-blockers, clonidine, guanethidine, and reserpine): Increased frequency of glucose monitoring may be required (7).

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 10/2019

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FULL PRESCRIBING INFORMATION

INSTRUCTIONS AND USAGE
FIASP® is indicated to improve glycemic control in adults with diabetes mellitus.

DOSE AND ADMINISTRATION

2.1 Important Administration Instructions

- Always check insulin label before administration [see Warnings and Precautions (5.4)].
- Inspect FIASP® visually before use. It should appear clear and colorless. Do not use FIASP® if particulate matter or coloration is seen.
- Do not mix FIASP® with any other insulin.

2.2 Route of Administration Instructions

- Subcutaneous Injection:
  - Inject FIASP® at the start of a meal or within 20 minutes after starting a meal subcutaneously into the abdomen, upper arm, or thigh.
  - Rotate injection sites within the same region from one injection to the next to reduce the risk of lipodystrophy and localized cutaneous amyloidosis. Do not inject into areas of lipodystrophy or localized cutaneous amyloidosis [see Adverse Reactions (6.1, 6.3)].
- FIASP® given by subcutaneous injection should generally be used in regimens with intermediate or long-acting insulin [see Warnings and Precautions (5.2)].
- Instruct patients on basal-bolus treatment who forget a mealtime dose to monitor their blood glucose level to decide if an insulin dose is needed, and to reschedule their usual dosing schedule at the next meal.
- The FIASP® FlexTouch® pen dials in 1 unit increments.
- Use FIASP® FlexTouch® pen with caution in patients with visual impairment that may rely on audible clicks to dial their dose.

Continuous Subcutaneous Infusion (Insulin Pump):

- Refer to the continuous subcutaneous insulin infusion pump user manual to see if FIASP® can be used with the insulin pump. Use FIASP® in accordance with the insulin pump systems’ instructions for use.
- Administer FIASP® by continuous subcutaneous infusion in a region recommended in the instructions from the pump manufacturer. Rotate infusion sites within the same region to reduce the risk of lipodystrophy and localized cutaneous amyloidosis. Do not inject into areas of lipodystrophy or localized cutaneous amyloidosis [see Adverse Reactions (6.1)].
- Teach patients using continuous subcutaneous infusion therapy to administer insulin by injection and have alternate insulin therapy available in case of insulin pump failure [see Warnings and Precautions (5.8)].
- Change FIASP® in the pump reservoir at least every 6 days, or according to the pump user manual, whichever is shorter. Follow the FIASP®-specific information for in-use time because FIASP®-specific information may differ from general insulin pump user manual instructions.
- Change the infusion set and the infusion set insertion site according to the manufacturer’s user manual.
- Do not mix with other insulins or diluents in the insulin pump.
- Do not expose FIASP® in the pump reservoir temperatures greater than 98.6°F (37°C).

Intravenous Administration:

- Administer FIASP® intravenously only under medical supervision with close monitoring of blood glucose and potassium levels to avoid hyperglycemia and hypokalemia [see Warnings and Precautions (5.3, 5.5)].
- Dilute FIASP® to concentrations from 0.5 unit/mL to 1 unit/mL insulin aspart in infusion systems using polypropylene infusion bags.
- FIASP® is stable at room temperature for 24 hours in 0.9% sodium chloride or 5% dextrose infusion fluids [see How Supplied/Storage and Handling (16.2)].

2.3 Dosage Information

- Individualize the dosage of FIASP® based on the patient’s metabolic needs, blood glucose monitoring results, and glycemic control goal.
- If converting from another mealtime insulin to FIASP®, the initial change can be done on a unit-to-unit basis.
- Dose adjustments may be needed when switching from another insulin, with changes in physical activity, changes in concomitant medications, changes in meal pattern (i.e., macronutrient content or timing of food intake), changes in renal or hepatic function or during acute illness to minimize the risk of hypoglycemia or hyperglycemia [see Warnings and Precautions (5.2, 5.3) and Drug Interactions (7)].
- Closely monitor blood glucose when converting insulins used in insulin pumps. Significant individualization of insulin pump parameters may be necessary to minimize the risk of hypoglycemia and hyperglycemia [see Warnings and Precautions (5.2, 5.3) and Adverse Reactions (6.1)].
- During changes to a patient’s insulin regimen, increase the frequency of blood glucose monitoring [see Warnings and Precautions (5.2)].
- Dosage adjustment may be needed when FIASP® is coadministered with certain drugs [see Drug Interactions (7)].

3 DOSAGE FORMS AND STRENGTHS

- Injection: 100 units of insulin aspart per mL (U-100) is available as a clear and colorless solution in:
  - 10 mL multiple-dose vial
  - 3 mL single-patient-use FIASP® FlexTouch® pen
  - 3 mL single-patient-use PenFill® cartridges for use in a PenFill® cartridge-based device

4 CONTRAINDICATIONS

FIASP® is contraindicated:
- During episodes of hypoglycemia [see Warnings and Precautions (5.2)]
- In patients with known hypersensitivity to insulin aspart or one of the excipients in FIASP® [see Warnings and Precautions (5.6)].

5 WARNINGS AND PRECAUTIONS

5.1 Never Share a FIASP® FlexTouch® Pen, PenFill® Cartridge or PenFill® Cartridge Device Between Patients

FIASP® FlexTouch® disposable pen, PenFill® cartridge and PenFill® cartridge devices should never be shared between patients, even if the needle is changed. Patients using FIASP® vials should never share needles or syringes with another person. Sharing poses a risk for transmission of blood-borne pathogens.

5.2 Hypoglycemia or Hypoglycemia with Changes in Insulin Regimen

Changes in an insulin regimen (e.g., insulin strength, manufacturer, route of administration) may alter glycemic control and predispose to hypoglycemia [see Warnings and Precautions (5.3)] or hyperglycemia. Repeated insulin injections into areas of lipodystrophy or localized cutaneous amyloidosis have been reported to result in hyperglycemia; and a sudden change in the injection site (to an unaffected area) has been reported to result in hypoglycemia [see Adverse Reactions (6.1, 6.3)].

Make any changes to a patient’s insulin regimen under close medical supervision with increased frequency of blood glucose monitoring. Advise patients who have repeatedly injected into areas of lipodystrophy or localized cutaneous amyloidosis to change the injection site to unaffected areas and closely monitor for hypoglycemia. For patients with type 2 diabetes, dosage adjustments in concomitant oral anti-diabetic treatment may be needed.

5.3 Hyperglycemia

Hyperglycemia is the most common adverse reaction of all insulin therapies, including FIASP® [see Adverse Reactions (6.1)]. Severe hyperglycemia can cause seizures, may lead to unconsciousness, may be life-threatening, or cause death. Hyperglycemia can impair concentration ability and reaction time; this may place an individual and others at risk in situations where these abilities are important (e.g., driving or operating other machinery). FIASP® or any insulin, should not be used during episodes of hyperglycemia [see Contraindications (4)].

Hyperglycemia can happen suddenly and symptoms may differ in each individual and change over time in the same individual. Symptomatic awareness of hyperglycemia may be less pronounced in patients with longstanding diabetes, in patients with diabetic nerve disease, in patients using medications that block the sympathetic nervous system (e.g., beta-blockers) [see Drug Interactions (7)], or in patients who experience recurrent hyperglycemia.

Risk Factors for Hyperglycemia

The risk of hyperglycemia after an injection is related to the duration of action of the insulin and, in general, is highest when the glucose lowering effect of the insulin is maximal. The timing of hyperglycemia usually reflects the time-action profile of the administered insulin formulation. As with all insulin preparations, the glucose lowering effect of FIASP® may vary in different individuals or at different times in the same individual and depends on many conditions, including the area of injection as well as the injection site blood supply and temperature [see Clinical Pharmacology (12.3)].

Other factors, which may increase the risk of hyperglycemia include changes in diet (e.g., macronutrient content or timing of meals), changes in level of physical activity, or changes to co-administered medication [see Drug Interactions (7)]. Patients with renal or hepatic impairment may be at higher risk of hyperglycemia [see Use in Specific Populations (8.6, 8.7)].

5.4 Hypoglycemia Due to Medication Errors

Accidental mix-ups between insulin products have been reported. To avoid medication errors between FIASP® and other insulins, instruct patients to always check the insulin label before each injection.

5.5 Hypokalemia

All insulin products, including FIASP®, can cause a shift in potassium from the extracellular to intracellular space, possibly leading to hypokalemia. Untreated hypokalemia may cause respiratory paralysis, ventricular arrhythmia and death. Monitor potassium levels to avoid hypokalemia and patients who have reduced symptomatic awareness of hypoglycemia, increased frequency of blood glucose monitoring is recommended.

5.6 Hypersensitivity and Allergic Reactions

Severe, life-threatening, generalized allergy, including anaphylaxis, can occur with insulin products, including FIASP® [see Adverse Reactions (6.1)]. Patients with a history of anaphylaxis to insulin, and other allergies, may have hypersensitivity reactions to insulin aspart, or one of the excipients in FIASP® [see Contraindications (4)].

5.7 Fluid Retention and Heart Failure with Concomitant Use of PPAR-Gamma Agonists

Thiazolidinediones (TZDs), which are peroxisome proliferator-activated receptor (PPAR)-gamma agonists, can cause dose-related fluid retention, particularly when used in combination with insulin. Fluid retention may lead to or exacerbate heart failure. Patients treated with insulin, including FIASP®, and a PPAR-gamma agonist should be observed for signs and symptoms of heart failure. If heart failure develops, it should be managed according to current standards of care, and discontinuation or dose reduction of the PPAR-gamma agonist must be considered.

5.8 Hyperglycemia and Ketoacidosis Due to Insulin Pump Device Malfunction

Pump or infusion set malfunctions can lead to a rapid onset of hyperglycemia and ketoadiposopathy. Prompt identification and correction of the cause of hyperglycemia or ketosis is necessary. Interim therapy with subcutaneous injection of FIASP® may be required. Patients using continuous subcutaneous insulin infusion pumps must be trained to administer insulin by injection and have alternate insulin therapy available in case of pump failure [see Dosage and Administration (2.2), How Supplied/Storage and Handling (16.2), and Patient Counseling Information (17)].

6 ADVERSE REACTIONS

The following adverse reactions are also discussed elsewhere:

- Hypoglycemia [see Warnings and Precautions (5.3)]
- Hypokalemia [see Warnings and Precautions (5.5)]
- Hypersensitivity and allergic reactions [see Warnings and Precautions (5.6)]

6.1 Clinical Trial Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug, and may not reflect the rates actually observed in clinical practice.

The data in Table 1 reflect the exposure of 763 patients with type 1 diabetes to FIASP® in one clinical trial with a mean exposure duration of 25 weeks [see Clinical Studies (14)]. The mean age was 44.4 years and the mean duration of diabetes was 19.9 years. 59% were male, 93% were Caucasian, 2% were Black or African American.
American and 7% were Hispanic. The mean BMI was 26.7 kg/m² and the mean HbA₁c at baseline was 7.5%.

The data in Table 2 reflect the exposure of 341 patients with type 2 diabetes to FIASP® in one clinical trial with a mean exposure duration of 24 weeks [see Clinical Studies (14)]. The mean age was 59.6 years and the mean duration of diabetes was 13.2 years. 47% were male, 80% were Caucasian, 6% were Black or African American and 8% were Hispanic. The mean BMI was 31.5 kg/m² and the mean HbA₁c at baseline was 8.0%.

Common adverse reactions, excluding hypoglycemia, were defined as events occurring in ≥5% and occurring at the same rate or greater for FIASP®-treated subjects than comparator-treated subjects.

Table 1. Adverse Reactions (%) in Patients with Type 1 Diabetes

<table>
<thead>
<tr>
<th>Condition</th>
<th>FIASP® + insulin detemir (N=336)</th>
<th>Postmeal FIASP® + insulin detemir (N=377)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasopharyngitis</td>
<td>20.2</td>
<td>23.9</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>9.1</td>
<td>7.4</td>
</tr>
<tr>
<td>Nausea</td>
<td>4.9</td>
<td>5.0</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>5.4</td>
<td>3.2</td>
</tr>
<tr>
<td>Back pain</td>
<td>5.2</td>
<td>4.0</td>
</tr>
</tbody>
</table>

*Incidence ≥ 5% and occurring at the same rate or greater with FIASP® than comparator

Table 2. Adverse Reactions (%) in Patients with Type 2 Diabetes

<table>
<thead>
<tr>
<th>Condition</th>
<th>FIASP® + insulin glargine (N=341)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary tract infection</td>
<td>5.9</td>
</tr>
</tbody>
</table>

*Incidence ≥ 5% and occurring at the same rate or greater with FIASP® than comparator

**Hypoglycemia**

Hypoglycemia is the most commonly observed adverse reaction in patients using insulin, including FIASP®. The rates of reported hypoglycemia depend on the definition of hypoglycemia used, diabetes type, insulin dose, intensity of glucose control, background therapies, and other intrinsic and extrinsic patient factors. For these reasons, comparing rates of hypoglycemia in clinical trials for FIASP® with the incidence of hypoglycemia for other products may be misleading and also, may not be representative of hypoglycemia rates that occur in clinical practice.

Incidence rates for severe hypoglycemia in adults with type 1 and type 2 diabetes mellitus treated with FIASP® in clinical trials are shown in Table 3 [see Clinical Studies (14)].

Table 3. Proportion (%) of Patients with Type 1 Diabetes and Type 2 Diabetes Experiencing at Least One Episode of Severe Hypoglycemia in Adult Clinical Trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Type 1 (%)</th>
<th>Type 2 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study A (Type 1)</td>
<td>7.3</td>
<td>3.4</td>
</tr>
<tr>
<td>Study B (Type 2)</td>
<td>7.3</td>
<td>3.4</td>
</tr>
<tr>
<td>Study C (Type 2)</td>
<td>7.3</td>
<td>3.4</td>
</tr>
<tr>
<td>Study D (Type 2) (CSII)</td>
<td>7.3</td>
<td>3.4</td>
</tr>
</tbody>
</table>

Severe hypoglycemia: an episode requiring assistance of another person to actively administer carbohydrate, glucagon, or other resuscitative actions

In Study D, patients with type 1 diabetes treated with FIASP® in a pump reported a higher rate of blood glucose confirmed hypoglycemic episodes (where self-measured glucose calibrated to plasma was less than 36 mg/dL) within first hour after a meal compared to patients treated with detemir [see Clinical Trials (44)].

**Allergic Reactions**

Severe, life-threatening, generalized allergy, including anaphylaxis, generalized skin reactions, angioedema, bronchospasm, hypotension, and shock may occur with any insulin, including FIASP®, and may be life-threatening. In the clinical program, generalized hypersensitivity reactions (manifested by generalized skin rash and facial edema) were reported in 0.4% of patients treated with FIASP®. Allergic skin manifestations reported with FIASP® in 1.7% of patients from the clinical program include eczema, rash, rash pruritic, urticaria and dermatis. In Study D, allergic reactions were reported in 4.2% of patients with type 1 diabetes treated with FIASP®.

**Lipoatrophy**

Administration of insulin, including FIASP®, has resulted in lipoatrophy (enlargement or thickening of tissue) and lipoatrophy (depression in tissue). In the clinical program, lipoatrophy has been reported in 0.4% of patients treated with FIASP® [see Dosage and Administration (2.2)].

**Injection/Infusion Site Reactions**

As with other insulin therapy, patients may experience rash, redness, inflammation, pain, bruising or itching at the site of FIASP® injection or infusion. These reactions usually resolve in a few days but in some occasions, may require discontinuation of FIASP®. In the clinical program, injection site reactions occurred in 1.6% of patients treated with FIASP®. In Study A, patients with type 1 diabetes treated with FIASP® reported 2.2% injection site reactions. In Study D, infusion site reactions were reported in 10.2% of patients with type 1 diabetes treated with FIASP®.

**Weight Gain**

Weight gain can occur with insulin therapy, including FIASP®, and has been attributed to the anabolic effects of insulin and the increase in glucosuria. In Study A, patients with type 1 diabetes treated with FIASP® gained an average of 0.7 kg and in Study B, patients with type 2 diabetes treated with FIASP® gained an average of 2.7 kg.

**Peripheral Edema**

Insulin, including FIASP®, may cause sodium retention and edema, particularly if previous poor metabolic control is improved by intensified insulin therapy. In the clinical program, peripheral edema occurred in 0% of patients treated with FIASP®.

**6.2 Immunogenicity**

As with all therapeutic proteins, there is a potential for immunogeneity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay and may be influenced by several factors such as: assay methodology, sample handling, timing of sample collection, concomitant medication, and underlying disease. For these reasons, comparison of the incidence of antibodies to FIASP® in the studies described below with the incidence of antibodies in other studies or to other products may be misleading.

In a 26-week study in adult subjects with type 1 diabetes (Study A [see Clinical Studies (14)], among the 763 subjects who received FIASP® at least once during the study, 10.3% of patients positive for antibodies (AIA) at least once during the study, including 90.3% that were positive at baseline. A total of 24.8% of patients who received FIASP® were positive for anti-drug (insulin aspart) antibodies (ADA) at least once during the study, including 17.3% that were positive at baseline.

**6.3 Postmarketing Experience**

The following additional adverse reactions have been identified during post-approval use of insulin aspart. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Localized cutaneous amyloidosis at the injection site has occurred. A causal relationship to drug exposure is always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

**8 USE IN SPECIFIC POPULATIONS**

**8.1 Pregnancy**

There are no available data with FIASP® in pregnant women to inform a drug-associated risk for major birth defects and miscarriage. Available information from published randomized controlled trials with insulin aspart use during the second trimester of pregnancy have not revealed any increased risk of major birth defects or adverse maternal or fetal outcomes [see Data]. There are risks to the mother and fetus associated with poorly controlled diabetes in pregnancy [see Clinical Considerations].

In animal reproduction studies, administration of subcutaneous insulin aspart to pregnant rats and rabbits during the period of organogenesis did not cause adverse developmental effects at exposures 8- times and equal to the human subcutaneous dose of 1.0 unit/kg/day, respectively. Pre- and post-implantation losses and visceral/skeletal abnormalities were seen at higher exposures, which are considered secondary to maternal hypoglycemia. These effects were similar to those observed in rats administered regular human insulin [see Data].

The estimated background risk of major birth defects is 6-10% in women with pre-gestational diabetes with a HbA₁c > 7%, and has been reported to be as high as 20-25% in women with a HbA₁c > 10%. The estimated background risk of miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2.4% and 15-20%, respectively.

**Clinical Considerations**

**Disease-Associated Maternal and/or Embryo-Fetal Risk**

Poorly controlled diabetes in pregnancy increases the maternal risk for diabetic ketoacidosis, preeclampsia, spontaneous abortions, premature deliveries and fetal complications. Poorly controlled diabetes increases the fetal risk for major birth defects, stillbirth, and macrosomia related morbidity.

**Data**

**Human Data**

Published data from 5 randomized controlled trials of 441 pregnant women with diabetes mellitus treated with insulin aspart starting during the late 2nd trimester of pregnancy did not identify an association of insulin aspart with major birth defects or adverse maternal or fetal outcomes. However, these studies cannot definitely establish the absence of any risk because of methodological limitations, including a variable duration of treatment and small size and limitations of the majority of the trials.

**Animal Data**

Fertility, embryo-fetal and pre-and postnatal development studies have been performed with insulin aspart and regular human insulin in rats and rabbits. In a combined fertility and embryo-fetal development study in rats, insulin aspart was administered before mating, during mating and throughout pregnancy. Further, in a pre- and postnatal development study insulin aspart was given throughout pregnancy and during lactation to rats. In an embryo-fetal development study insulin aspart was given to female rabbits during organogenesis. The effects of insulin aspart did not differ from those observed with subcutaneous regular human insulin. Insulin aspart, like human insulin, caused pre- and post-implantation losses and visceral/skeletal abnormalities in rats at a dose of 200 units/kg/day (approximately 32 times the human subcutaneous dose of 1.0 unit/kg/day, based on human exposure equivalents) and in rabbits at a dose of 10 units/kg/day (approximately three times the human subcutaneous dose of 1.0 unit/kg/day, based on human exposure equivalents). No significant effects were observed in rats at a dose of 50 units/kg/day and in rabbits at a dose of 3 units/
kg/day. These doses are approximately 8 times the human subcutaneous dose of 1.0 unit/kg/day for rats and equal to the human subcutaneous dose of 1.0 unit/kg/day for rabbits, based on human exposure equivalents. The effects are considered secondary to maternal hypoglycemia.

8.2 Lactation
Risk Summary
There are no data on the presence of FIASP® in human milk, the effects on the breastfed infant, or the effect on milk production. One small published study reported that exogenous insulin, including insulin aspart, was present in human milk. However, there is insufficient information to determine the effects of insulin aspart on the breastfed infant and no available information on the effects of insulin aspart on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for insulin, any potential adverse effects on the breastfed child from FIASP® or insulin aspart or from the underlying maternal condition.

8.4 Pediatric Use
The safety and effectiveness of FIASP® in pediatric patients have not been established.

8.5 Geriatric Use
In the three controlled clinical studies, 192 of 1219 (16%) FIASP® treated patients with type 1 or type 2 diabetes were ≥65 years of age and 24 of 1219 (2%) were ≥75 years of age. No overall differences in safety or effectiveness were observed between these elderly patients and younger adult patients.

Nevertheless, caution should be exercised when FIASP® is administered to geriatric patients. In elderly patients with diabetes, the initial dosing, dose adjustments, and maintenance dosage should be conservative to avoid hypoglycemia [see Warnings and Precautions (5.3), Adverse Reactions (6.1) and Clinical Studies (14)].

Pharmacokinetic/pharmacodynamic study to assess the effect of age on the onset of FIASP® action has been performed [see Clinical Pharmacology (12.3)].

8.6 Renal Impairment
Patients with renal impairment may be at increased risk of hypoglycemia and may require more frequent FIASP® dose adjustment and more frequent blood glucose monitoring [see Warnings and Precautions (5.3) and Clinical Pharmacology (12.3)].

8.7 Hepatic Impairment
Patients with hepatic impairment may be at increased risk of hypoglycemia and may require more frequent FIASP® dose adjustment and more frequent blood glucose monitoring [see Warnings and Precautions (5.3) and Clinical Pharmacology (12.3)].

10 OVERDOSAGE
Excess insulin administration may cause hypoglycemia and hypokalemia [see Warnings and Precautions (5.3, 5.5)]. Mild episodes of hypoglycemia usually can be treated with oral glucose. Adjustments in drug dosage, meal patterns, and exercise, may be needed. More severe episodes with coma, seizure or hypoglycemia must be corrected appropriately.

Sustained carbohydrate intake and observation may be necessary. More severe episodes of hypoglycemia usually can be treated with oral glucose. Adjustments in drug dosage, meal patterns, or exercise, may be needed. More severe episodes with coma, seizure or hypoglycemia must be corrected appropriately.

12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
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.

12.2 Pharmacodynamics
The time course of insulin action (i.e., glucose lowering) may vary considerably in different individuals or within the same individual. The average pharmacodynamic profile (i.e., glucose lowering effect measured as glucose infusion rate (GIR) in a euglycemic clamp study) for subcutaneous administration of 0.1, 0.2, and 0.4 unit/kg of FIASP® in 46 patients with Type 1 diabetes is shown in Figure 2 and key characteristics of the timing of the effect are described in Table 5 below.

Table 5. Timing of insulin effect (i.e., mean pharmacodynamic effect) after subcutaneous administration of 0.1, 0.2 and 0.4 unit/kg of FIASP® in patients (N=46) with Type 1 Diabetes and corresponding to the data shown in Figure 2

<table>
<thead>
<tr>
<th>Parameter for Insulin Effect</th>
<th>FIASP® 0.1 unit/kg</th>
<th>FIASP® 0.2 unit/kg</th>
<th>FIASP® 0.4 unit/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to first measurable effect (minutes)</td>
<td>-20</td>
<td>-17</td>
<td>-16</td>
</tr>
<tr>
<td>Time to peak effect (minutes)</td>
<td>-312</td>
<td>-322</td>
<td>-133</td>
</tr>
<tr>
<td>Time for effect to return to baseline (hours)</td>
<td>-5</td>
<td>-6</td>
<td>-7</td>
</tr>
</tbody>
</table>

Figure 2. Mean insulin effect (i.e., mean pharmacodynamic effect) over time after subcutaneous administration of 0.1, 0.2 and 0.4 unit/kg of FIASP® in patients (N=46) with Type 1 diabetes

On average, the pharmacodynamic effects of FIASP®, measured as area under the glucose infusion rate-time curve (AUCmin), were 657 mg.kg/day, 1406 mg.kg/day, and 2427 mg.kg/day following administration of 0.1, 0.2, and 0.4 unit/kg of FIASP®.

The day-to-day variability in glucose-lowering effect of FIASP® within patients was ~18% for total glucose lowering (AUCmin, 0-24h) and ~19% for maximum glucose lowering effect (GIRmax).

12.3 Pharmacokinetics
Absorption
Pharmacokinetic results from a euglycemic clamp study in adult patients with type 1 diabetes (N=51) showed that insulin aspart appeared in the circulation ~25 minutes after administration of FIASP® (Figure 3). Time to maximum insulin concentrations was achieved ~65 minutes after administration of FIASP®.

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
In 52-week studies, Sprague-Dawley rats were dosed subcutaneously with insulin aspart at 10, 50, and 200 units/kg/day (approximately 2, 8, and 32 times the human subcutaneous dose of 1.0 unit/kg/day, based on units/body surface area, respectively). At a dose of 200 units/kg/day, insulin aspart increased the incidence of mammary gland tumors in females when compared to untreated controls. The incidence of mammary tumors for insulin aspart was not significantly different than for regular human insulin. The relevance of these findings to humans is not known.

Insulin aspart was not genotoxic in the following tests: Ames test, mouse lymphoma cell forward gene mutation test, human peripheral blood lymphocyte chromosome aberration test, in vivo micronucleus test in mice, and in vivo UDS test in rat liver hepatocytes. In fertility studies in male and female rats, at subcutaneous doses up to 200 units/kg/day (approximately 32 times the human subcutaneous dose, based on units/body surface area), no direct adverse effects on male and female fertility, or general reproductive performance of animals was observed.

14 CLINICAL STUDIES
14.1 Overview of Clinical Studies
The efficacy of FIASP® was evaluated in 3 randomized, active-controlled trials of 18 to 26 weeks duration. In total 1224 adult subjects were randomized to FIASP® (N=763 with type 1 diabetes; N=461 with type 2 diabetes). In adult patients with type 1 diabetes, mealtime FIASP® and postmeal FIASP® led to non-inferior glycemic control compared to metformine NovoLog®, both in combination with insulin detemir. In adult patients with type 2 diabetes, mealtime FIASP® provided non-inferior glycemic control compared to metformine NovoLog®, both in combination with metformin. In addition, mealtime FIASP® in a basal-bolus regimen with metformin also provided statistically significant improvement.
in the overall glyemic control compared to basal insulin therapy alone with metformin in adult patients with type 2 diabetes.

In adults with type 1 diabetes (N=472), FIAP® led to non-inferior glyemic control compared to NovoLog® when both were administered by continuous subcutaneous insulin infusion (CSII) pump.

14.2 Type 1 Diabetes – Adults

Study A (NCT01831765): FIAP® added to insulin detemir in patients with Type 1 DM inadequately controlled at baseline.

The efficacy of FIAP® was evaluated in a 26-week, randomized, active controlled, treat-to-target, multicenter trial in 1143 adult patients with type 1 diabetes inadequately controlled at baseline. Patients were randomized to either blinded mealtime FIAP® (N=381), blinded mealtime NovoLog® (N=380), or open-label postmeal FIAP® (N=382), all in combination with once or twice daily insulin detemir. At randomization, patients were switched to FIAP® on a unit to unit basis. Mealtine FIAP® or NovoLog® was injected 0-2 minutes before the meal, and postmeal FIAP® was injected 20 minutes after the start of the meal.

The mean age of the randomized subjects was 44.4 years and mean duration of diabetes was 19.9 years. 59% were male, 93% were White, 2% were Black or African American, and 7% were Hispanic. The mean BMI was 26.7 kg/m².

After 26 weeks of treatment, treatment difference in HbA1c was similar among study arms at the end of the trial. The mean BMI was 31.2 kg/m² in Hispanic. The mean BMI was 26.3 kg/m² in White, 2% were Black or African American, and 7% were Hispanic. The mean BMI was 30.8 kg/m² in Hispanic.

After 18 weeks of treatment, addition of FIAP® to basal insulin and metformin statistically significantly reduced HbA1c compared to continuing basal insulin and metformin therapy without addition of FIAP®. The basal insulins used in both treatment arms were insulin glargine, insulin detemir or NPH. All patients were also required to be on at least 10 mg metformin treatment at baseline.

The mean age of the trial population was 57.4 years and the mean duration of diabetes was 11.3 years. 48% were male, 70% were White, 4% were Black or African American, and 37% were Hispanic. The mean BMI was 30.8 kg/m² in Hispanic.

After 18 weeks of treatment, addition of FIAP® to basal insulin and metformin statistically significantly reduced HbA1c compared to continuing basal insulin and metformin therapy without addition of FIAP®. The basal insulins used in both treatment arms were insulin glargine, insulin detemir or NPH. All patients were also required to be on at least 10 mg metformin treatment at baseline.

14.3 Type 2 Diabetes – Adults

Study B (NCT01819129): FIAP® added to basal insulin and oral antidiabetics in patients with Type 2 DM inadequately controlled at baseline on basal insulin and oral antidiabetics.

The efficacy of FIAP® was evaluated in a 26-week, randomized, double-blind, active controlled, treat-to-target, multicenter, multinational, parallel group trial in 689 adult patients with type 2 diabetes who were inadequately controlled at baseline on basal insulin and oral antidiabetic therapy and had been on these therapies for at least 6 months. Patients were randomized to either mealtime FIAP® or to mealtime NovoLog®, both in combination with insulin glargine and metformin in a basal-bolus regimen. Mealtine FIAP® or mealtime NovoLog® was injected 0-2 minutes before the meal.

The mean age of the randomized subjects was 59.5 years and the mean duration of diabetes was 12.7 years. 49% were male, 81% were White, 6% were Black or African American, and 6% were Hispanic. The mean BMI was 31.2 kg/m².

After 26 weeks of treatment, the treatment difference in HbA1c reduction from baseline between mealtime FIAP® and mealtime NovoLog®, both in combination with insulin glargine and metformin, met the pre-specified non-inferiority margin (0.4%). See Table 7. Insulin doses were similar among study arms at the end of the trial.

16. HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

FIAP® (insulin aspart injection) 100 units of insulin aspart per mL (U-100) is available as a clear and colorless solution in the following presentations and packaging configurations:

- Carton of 10 mL multiple-dose vials
- NDC 0169-3201-11
- Carton of 5 mL single-patient use
- NDC 0169-3204-15
- FIASP® FlexTouch® pens
- NDC 0169-3205-10
- Penfill® cartridges

*FIAP® Penfill® cartridges are designed for use with Novo Nordisk insulin delivery devices.

16.2 Recommended Storage

No special storage conditions are required. Unused FIAP® vials should be stored between 2° to 8°C (36° to 46°F) in a refrigerator, but not in or near a freezing compartment. FIAP® should not be exposed to excessive heat or light and must never be frozen. Do not freeze FIAP® and do not use FIAP® if it has been frozen. FIAP® should not be drawn into a syringe and stored for later use. Only use the product if it has a clear and almost colorless appearance.

Keep the cap on the pen in order to protect from light. Keep unused vials and FIAP® FlexTouch® in the carton so they will stay clean and protected from light.

Always remove the needle after each injection and store FIAP® FlexTouch® without a needle attached. This prevents contamination and/or infection, or leakage of insulin, and will ensure accurate dosing. Always use a new needle for each injection to prevent contamination.

The storage conditions for vials, FIAP® FlexTouch® pens, and 3 mL single-patient use cartridges are summarized in Table 10.

10. Table 10. Storage Conditions for Vial, FIAP® FlexTouch, and Penfill® Cartridges

<table>
<thead>
<tr>
<th>Storage Condition</th>
<th>FIASP®</th>
<th>Penfill®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Room Temperature</td>
<td>Below 30°C</td>
<td>Below 30°C</td>
</tr>
<tr>
<td>Refrigerated</td>
<td>2°C to 8°C</td>
<td>2°C to 8°C</td>
</tr>
<tr>
<td>10 mL multiple-dose vial</td>
<td>28 days</td>
<td>28 days*</td>
</tr>
<tr>
<td>3 mL single-patient use FIASP® FlexTouch® pen</td>
<td>28 days</td>
<td>28 days*</td>
</tr>
<tr>
<td>3 mL single-patient use Penfill® cartridges</td>
<td>28 days</td>
<td>28 days</td>
</tr>
</tbody>
</table>

*For insulin pump use, the total in-use time is 28 days, including 6 days pump in-use time.

Storage of FIAP® in Insulin Pumps:

FIAP® in the pump reservoir should be replaced at least every 6 days, or according to the pump user manual, whichever is shorter, to avoid insulin degradation or after exposure to temperatures that exceed 37°C (98.6°F). The infusion set and infusion set insertion sites should be changed according to the manufacturers’ user manual.
Storage of FIASP® in Intravenous Infusion Fluids:
Infusion bags prepared as indicated under Dosage and Administration (2.2) are stable at room temperature for 24 hours.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-Approved Patient Labeling (Patient Information and Instructions for Use).

Never Share a FIASP® FlexTouch® Pen Device, PenFill® Cartridge or PenFill® Cartridge Device Between Patients

Advise patients that they should never share a FIASP® FlexTouch® pen device, PenFill® cartridge or PenFill® cartridge devices with another person, even if the needle is changed, because doing so carries a risk for transmission of blood-borne pathogens. Advise patients using FIASP® vials not to share needles or syringes with another person. Sharing poses a risk for transmission of blood-borne pathogens [see Warnings and Precautions (5.1)].

Hyperglycemia or Hypoglycemia

Inform patients that hypoglycemia is the most common adverse reaction with insulin. Instruct patients on self-management procedures including glucose monitoring, proper injection technique, and management of hypoglycemia and hyperglycemia, especially at initiation of FIASP® therapy. Instruct patients on handling of special situations such as intercurrent conditions (illness, stress, or emotional disturbances), an inadequate or skipped insulin dose, inadvertent administration of an increased insulin dose, inadequate food intake, and skipped meals. Instruct patients on the management of hyperglycemia [see Warnings and Precautions (5.3)].

Inform patients that their ability to concentrate and react may be impaired as a result of hypoglycemia. Advise patients who have frequent hypoglycemia or reduced or absent warning signs of hypoglycemia to use caution when driving or operating machinery.

Advise patients that changes in insulin regimen can predispose to hyperglycemia or hypoglycemia and that changes in insulin regimen should be made under close medical supervision [see Warnings and Precautions (5.2)].

Hypersensitivity Reactions

Advise patients that hypersensitivity reactions have occurred with FIASP®. Inform patients on the symptoms of hypersensitivity reactions [see Warnings and Precautions (5.6)].

Hypoglycemia due to Medication Errors

Instruct patients to always check the insulin label before each injection to avoid mix-ups between insulin products.

Patients Using Continuous Subcutaneous Insulin Pumps

• Train patients in intensive insulin therapy with multiple injections and in the function of their pump and pump accessories.
• Instruct patients to follow healthcare provider recommendations when setting basal and meal time infusion rate.
• Refer to the continuous subcutaneous infusion pump user manual to see if FIASP® can be used with the pump. See recommended reservoir and infusion sets in the insulin pump user manual.
• Instruct patients to replace insulin in the reservoir at least every 6 days, or according to the pump user manual, whichever is shorter; infusion sets and infusion set insertion sites should be changed in accordance with the manufacturers’ user manual. By following this schedule, patients avoid insulin degradation, infusion set occlusion, and loss of the insulin preservative.
• Instruct patients to discard insulin exposed to temperatures higher than 37°C (98.6°F).
• Instruct patients to inform physician and select a new site for infusion if infusion site becomes erythematous, pruritic, or thickened.
• Instruct patients on the risk of rapid hyperglycemia and ketosis due to pump malfunction, infusion set occlusion, leakage, disconnection or kinking, and degraded insulin. Instruct patients on the risk of hypoglycemia from pump malfunction. If these problems cannot be promptly corrected, instruct patients to resume therapy with subcutaneous insulin injection and contact their physician [see Warnings and Precautions (5) and How Supplied/Storage and Handling (16.2)].
Do not share your FIASP® with other people, even if the needle has been changed. You may give other people a serious infection, or get a serious infection from them.

What is FIASP®?
- FIASP® is a man-made insulin that is used to control high blood sugar in adults with diabetes mellitus.
- It is not known if FIASP® is safe and effective in children.

Who should not take FIASP®?
Do not take FIASP® if you:
- are having an episode of low blood sugar (hypoglycemia).
- have an allergy to insulin aspart or any of the ingredients in FIASP®.
- have kidney problems.
- have liver problems.
- are pregnant or plan to become pregnant. Talk with your healthcare provider about the best way to control your blood sugar if you plan to become pregnant or while you are pregnant.
- are breastfeeding or plan to breastfeed. It is not known if FIASP® passes into your breast milk. Talk with your healthcare provider about the best way to feed your baby while using FIASP®.
- are taking new prescription or over-the-counter medicines, vitamins, or herbal supplements.

Before taking FIASP®, tell your healthcare provider about all your medical conditions, including, if you:
- have kidney problems.
- have liver problems.
- are having an episode of low blood sugar (hypoglycemia).
- have an allergy to insulin aspart or any of the ingredients in FIASP®.
- are taking new prescription or over-the-counter medicines, vitamins, or herbal supplements.

Before you start taking FIASP®, talk to your healthcare provider about low blood sugar and how to manage it.

How should I take FIASP®?
- Read the Instructions for Use that come with your FIASP®.
- Take FIASP® exactly as your healthcare provider tells you to.
- FIASP® starts acting fast. You should take your dose of FIASP® at the beginning of the meal or within 20 minutes after starting a meal.
- Know the type and strength of insulin you take. Do not change the type of insulin you take unless your healthcare provider tells you to. The amount of insulin and the best time for you to take your insulin may need to change if you take different types of insulin.
- If you miss a dose of FIASP®, monitor your blood sugar levels to decide if an insulin dose is needed. Continue with your regular dosing schedule at the next meal.
- Check your blood sugar levels. Ask your healthcare provider what your blood sugars should be and when you should check your blood sugar levels.
- Do not reuse or share needles with other people. You may give other people a serious infection or get a serious infection from them.
- FIASP® can be injected under the skin (subcutaneously) of your stomach area, upper legs, or upper arms, or by continuous infusion under the skin (subcutaneously) through an insulin pump into an area of your body recommended in the instructions that come with your insulin pump.
- Change (rotate) your injection sites within the area you choose with each dose to reduce your risk of getting lipodystrophy (pits in skin or thickened skin) and localized cutaneous amyloidosis (skin with lumps) at the injection sites.
- Do not use the same exact spot for each injection.
- Do not inject where the skin has pits, is thickened, or has lumps.
- Do not inject where the skin is tender, bruised, scaly or hard, or into scars or damaged skin.

What should I avoid while taking FIASP®?
While taking FIASP® do not:
- Drive or operate heavy machinery until you know how FIASP® affects you.
- Drink alcohol or use prescription or over-the-counter medicines that contain alcohol.

What are the possible side effects of FIASP®?
FIASP® may cause serious side effects that can lead to death, including:
- low blood sugar (hypoglycemia). Signs and symptoms that may indicate low blood sugar include:
  - dizziness or light-headedness
  - anxiety, irritability, or mood changes
  - slurred speech
  - confusion
  - headache
  - fast heart beat
- low potassium in your blood (hypokalemia).
- serious allergic reactions (whole body reactions). Get emergency medical help right away, if you have any of these signs or symptoms of a severe allergic reaction:
  - a rash over your whole body, trouble breathing, a fast heartbeat, swelling of your face, tongue or throat, swelling, extreme drowsiness, dizziness, confusion.
- heart failure. Taking certain diabetes pills called TZDs (thiazolidinediones) with FIASP® may cause heart failure in some people. This can happen even if you have never had heart failure or heart problems before. If you already have heart failure it may get worse while you are taking TZDs with FIASP®. Your healthcare provider should monitor you closely while you are taking TZDs with FIASP®. Tell your healthcare provider if you have any new or worse symptoms of heart failure including:
  - Shortness of breath, swelling of your ankles or feet, sudden weight gain.
  - Swelling of your ankles or feet, sudden weight gain.

Common side effects of FIASP® may include:
- skin problems such as eczema, rash, itching, redness and swelling of your skin (dermatitis)
- reactions at the injection site such as itching, rash
- skin thickening or pits at the injection site (lipodystrophy)
- weight gain

These are not all the possible side effects of FIASP®. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of FIASP®:
Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. You can ask your pharmacist or healthcare provider for information about FIASP® that is written for health professionals. Do not use FIASP® for a condition for which it was not prescribed. Do not give FIASP® to other people, even if they have the same symptoms that you have. It may harm them.

What are the ingredients in FIASP®?
Active Ingredient: insulin aspart
Inactive Ingredients: glycerol, phenol, metacresol, zinc, disodium phosphate dihydrate, arginine hydrochloride, niacinamide and water for injections

Manufactured by:
Novo Nordisk A/S
DK-2880 Bagsvaerd, Denmark

For more information, go to www.novonordisk-us.com or call 1-800-727-6500.

This Patient Information has been approved by the U.S. Food and Drug Administration. Revised: 10/2019
Instructions for Use
FIASP® (fee’ asp) FlexTouch® Pen
(insulin aspart injection)

• Do not share your FIASP® FlexTouch® Pen with other people, even if the needle is changed. You may give other people a serious infection, or get a serious infection from them.

• FIASP® FlexTouch® Pen (“Pen”) is a prefilled disposable, single-patient-use pen containing 300 units of U-100 FIASP® (insulin aspart injection). You can inject from 1 to 80 units in a single injection. The units can be increased by 1 unit at a time.

• People who are blind or have vision problems should not use the Pen without help from a person trained to use the Pen.

• Do not use a syringe to remove FIASP® from the FlexTouch® Pen.

Supplies you will need to give your FIASP® injection:
• FIASP® FlexTouch® Pen
• a new NovoFine®, NovoFine® Plus or NovoTwist® needle
• alcohol swab
• a sharps container for throwing away used Pens and needles.
• insulin scale

Preparation of FIASP®

Preparing your FIASP® FlexTouch® Pen:
• Wash your hands with soap and water.
• Before you start to prepare your injection, check the FIASP® FlexTouch® pen label to make sure you are taking the right type of insulin. This is especially important if you take more than 1 type of insulin.
• FIASP® should look clear and colorless. Do not use FIASP® if it is thick, cloudy, or is colored.
• Do not use FIASP® past the expiration date printed on the label or 28 days after you start using the Pen.
• Always use a new needle for each injection to help ensure sterility and prevent blocked needles. Do not reuse or share needles with another person. You may give other people a serious infection, or get a serious infection from them.

NovoFine®

Outer needle cap 
Inner needle cap 
Needle 
Paper tab

NovoFine® Plus 

Outer needle cap 
Inner needle cap 
Needle  
Paper tab

NovoTwist® 

Outer needle cap 
Inner needle cap 
Needle 
Paper tab

Priming your FIASP®

Step 7:
• Turn the dose selector to select 2 units (See Figure H).

Step 8:
• 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 (See Figure I).

Step 9:
• Hold the Pen with the needle pointing up. Press and hold in the dose button until the dose counter shows “0”. The “0” must line up with the dose pointer.

• A drop of insulin should be seen at the needle tip (See Figure J).
  o If you do not see a drop of insulin, repeat steps 7 to 9, no more than 6 times.
  o If you still do not see a drop of insulin, change the needle and repeat steps 7 to 9.

Selecting your dose:

Step 10:
Check to make sure the dose selector is set at 0.

• Turn the dose selector to select the number of units you need to inject. The dose pointer should line up with your dose (See Figure K).
  o If you select the wrong dose, you can turn the dose selector forwards or backwards to the correct dose.
  o The even numbers are printed on the dial.
  o The odd numbers are shown as lines.

• The FIASP® FlexTouch® Pen insulin scale will show you how much insulin is left in your Pen (See Figure L).

• To see how much insulin is left in your FIASP® FlexTouch® Pen:
  o Turn the dose selector until it stops. The dose counter will line up with the number of units of insulin that is left in your Pen. If the dose counter shows 80, there are at least 80 units left in your Pen.
  o If the dose counter shows less than 80, the number shown in the dose counter is the number of units left in your Pen.
Giving your injection:

- Inject your FIASP® exactly as your healthcare provider has shown you. Your healthcare provider should tell you if you need to pinch the skin before injecting.
- You should take your dose of FIASP® at the start of a meal or within 20 minutes after starting a meal.
- FIASP® can be injected under the skin (subcutaneously) of your stomach area (abdomen), upper legs (thighs) or upper arms. Do not inject FIASP® into your muscle.
- Change (rotate) your injection sites within the area you choose for each dose to reduce your risk of getting lipodystrophy (pits in skin or thickened skin) and localized cutaneous amyloidosis (skin with lumps) at the injection sites.
- Do not use the same injection site for each injection.
- Do not inject where the skin has pits, is thickened, or has lumps. Do not inject where the skin is tender, bruised, scaly or hard, or into scars or damaged skin.

Step 11:

- Choose your injection site and wipe the skin with an alcohol swab. Let the injection site dry before you inject your dose (See Figure M).

Step 12:

- Insert the needle into your skin (See Figure N).
  - Make sure you can see the dose counter. Do not cover it with your fingers; this can stop your injection.

Step 13:

- Press and hold down the dose button until the dose counter shows “0” (See Figure O).
  - 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 slowly count to 6 (See Figure P). When the dose counter returns to “0”, you will not get your full dose until 6 seconds later.
  - If the needle is removed before you count to 6, you may see a stream of insulin coming from the needle tip.
  - If you see a stream of insulin coming from the needle tip you will not get your full dose. If this happens you should check your blood sugar levels more often because you may need more insulin.

Step 14:

- Pull the needle out of your skin (See Figure Q).
  - If you see blood after you take the needle out of your skin, press the injection site lightly with a piece of gauze or an alcohol swab. Do not rub the area.

Step 15:

- Carefully remove the needle from the Pen and throw it away (See Figure R).
  - Do not recap the needle. Recapping the needle can lead to needle stick injury.
  - If you do not have a sharps container, carefully slip the needle into the outer needle cap (See Figure S). Safely remove the needle and throw it away as soon as you can.
  - Do not store the Pen with the needle attached. Storing without the needle attached helps prevent leaking, blocking of the needle, and air from entering the Pen.

Step 16:

- Replace the Pen cap by pushing it straight on (See Figure T).

After your injection:

- Put your used FIASP® FlexTouch® Pen and needles in a FDA-cleared sharps disposal container right away after use. Do not throw away (dispose of) loose needles and Pens in your household trash.
- If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
  - made of a heavy-duty plastic
  - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out
  - upright and stable during use
  - leak-resistant
  - properly labeled to warn of hazardous waste inside the container
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. Do not reuse or share needles or syringes with another person. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA’s website at: http://www.fda.gov/safesharpsdisposal.
- Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. Do not recycle your used sharps disposal container.

How should I store my FIASP® FlexTouch® Pen?

Before use:
- Store unused FIASP® FlexTouch® Pens in the refrigerator at 36°F to 46°F (2°C to 8°C) or at room temperature below 86°F (30°C).
- Do not freeze FIASP®. Do not use FIASP® if it has been frozen.
- Unused Pens may be used until the expiration date printed on the label, if kept in the refrigerator.
- If FIASP® FlexTouch® Pens are stored at room temperature prior to first use, it should be used or thrown away within 28 days.

Pen in use:
- Store the Pen you are currently using without the needle attached at room temperature below 86°F (30°C) or in the refrigerator at 36°F to 46°F (2°C to 8°C) for up to 28 days.
- Keep FIASP® away from excessive heat or light.
- The FIASP® FlexTouch® Pen you are using is to be thrown away after 28 days, even if it still has insulin left in it and the expiration date has not passed.

General Information about the safe and effective use of FIASP®:
- Keep FIASP® FlexTouch® Pens and needles out of the reach of children.
- Always use a new needle for each injection.
- Do not share FIASP® FlexTouch® Pens or needles with other people. You may give other people a serious infection, or get a serious infection from them.

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

Manufactured by:
Novo Nordisk A/S
DK-2880 Bagsvaerd, Denmark

Revised: 10/2019
For more information go to www.FIASPflextouch.com

© 2019 Novo Nordisk
US19FSP0235 November 2019
Instructions for Use

FIASP® (fee’ asp)  
(insulin aspart injection)  
10 mL multiple-dose vial (100 units/mL, U-100)

Read this Instructions for Use before you start taking FIASP® and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment. The vial is not recommended for use by the blind or visually impaired without the assistance of a person trained in the proper use of the product and insulin syringe.

Do not reuse or share syringes or needles with other people. You may give other people a serious infection or get a serious infection from them.

Supplies you will need to give your FIASP® injection:

• a 10 mL FIASP® vial
• a U-100 insulin syringe and needle
• 2 alcohol swabs
• 1 sharps container for throwing away used needles and syringes. See “Disposing of your used needles and syringes” at the end of these instructions.

Preparing your FIASP® dose:

• Do not roll or shake the FIASP® vial. Shaking the FIASP® vial right before the dose is drawn into the syringe may cause bubbles or foam. This can cause you to draw up the wrong dose of insulin.
• The tamper-resistant cap should not be loose or damaged before the first use. Do not use if the tamper-resistant cap is loose or damaged before using FIASP® for the first time.
• Wash your hands with soap and water.
• Before you start to prepare your injection, check the FIASP® label to make sure that you are taking the right type of insulin. This is especially important if you use more than 1 type of insulin.
• Check that the FIASP® vial is not cracked or damaged. Do not use if the FIASP® vial is cracked or damaged.
• FIASP® should look clear and colorless. Do not use FIASP® if it is thick, cloudy, or is colored.
• Do not use FIASP® past the expiration date printed on the label.

Step 1: Pull off the tamper-resistant cap (See Figure A).

Step 2: Wipe the rubber stopper with an alcohol swab (See Figure B).

Step 3: Hold the syringe with the needle pointing up. Pull down on the plunger until the tip of the plunger reaches the line for the number of units for your prescribed dose (See Figure C).

Step 4: Push the needle through the rubber stopper of the FIASP® vial (See Figure D).

Step 5: Push the plunger all the way in. This puts air into the FIASP® vial (See Figure E).

Step 6: Turn the FIASP® vial and syringe upside down and slowly pull the plunger down until the tip of the plunger is a few units past the line for your dose (See Figure F).

Step 7: Slowly push the plunger up until the tip of the plunger reaches the line for your prescribed FIASP® dose (See Figure H).

Step 8: Check the syringe to make sure you have the right dose of FIASP®.

Step 9: Pull the syringe out of the rubber stopper on the vial (See Figure I).

Step 10: Choose your injection site and wipe the skin with an alcohol swab (See Figure J). Let the injection site dry before you inject your dose.

Step 11: Insert the needle into your skin. Push down on the plunger to inject your dose (See Figure K).

Step 12: Pull the needle out of your skin. After your injection you may see a drop of FIASP® at the needle tip. This is normal and does not affect the dose you just received (See Figure L).

After your injection:

• Do not recap the needle. Recapping the needle can lead to needle stick injury.

Disposing of your used needles and syringes:

Put your used insulin needles and syringes in a FDA-cleared sharps disposal container right away after use. Do not throw away (dispose of) loose needles and syringes in your household trash.

If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:

• made of a heavy-duty plastic;
• can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out;
• upright and stable during use;
• leak-resistant, and
• properly labeled to warn of hazardous waste inside the container.

When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. Do not reuse or share needles or syringes with another person. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA’s website at:

http://www.fda.gov/safesharpsdisposal

Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. Do not recycle your used sharps disposal container.

Giving your FIASP® injection:

• Inject your FIASP® exactly as your healthcare provider has shown you. Your healthcare provider should tell you if you need to pinch the skin before injecting.
• You should take your dose of FIASP® at the start of a meal or within 20 minutes after starting a meal.
• FIASP® can be injected under the skin (subcutaneously) of your stomach area, upper legs, or upper arms, infused in an insulin pump into an area of your body recommended in the instructions that come with your insulin pump, or given through a needle in your arm (intravenously) by your healthcare provider. Do not inject FIASP® into your muscle.
• If you use FIASP® in an insulin pump, you should change the infusion sets and the infusion set insertion site according to the pump manufacturers’ user manual. The insulin in the reservoir should be changed at least every 6 days even if you have not used all of the insulin.
• If you use FIASP® in an insulin pump, see your insulin pump manual for instructions or talk to your healthcare provider. Your healthcare provider should provide recommendations for appropriate basal and meal time infusion rates.
• Change (rotate) your injection sites within the area you choose for each dose to reduce your risk of getting lipodystrophy (pits in skin or thickened skin) and localized cutaneous amyloidosis (skin with lumps) at the injection sites. Do not use the same injection site for each injection.
• Do not inject where the skin has pits, is thickened, or has lumps. Do not inject where the skin is tender, bruised, scaly or hard, or into scars or damaged skin.
• Do not dilute or mix FIASP® with any other type of insulin products or solutions.

Step 13: Insert the needle into your skin. Push down on the plunger to inject your dose (See Figure J). Make sure you have injected all the insulin in the syringe.

Step 14: Press the plunger up until the tip of the plunger is a few units past the line for your dose (See Figure K).

Step 15: Make sure you have injected all the insulin in the syringe.

Step 16: Pull the needle out of your skin. After your injection you may see a drop of FIASP® at the needle tip. This is normal and does not affect the dose you just received (See Figure L).

Step 17: If you see blood after you take the needle out of your skin, press the injection site lightly with a piece of gauze or an alcohol swab. Do not rub the area.

Step 18: After your injection:

• Do not recap the needle. Recapping the needle can lead to needle stick injury.

Disposing of your used needles and syringes:

Put your used insulin needles and syringes in a FDA-cleared sharps disposal container right away after use. Do not throw away (dispose of) loose needles and syringes in your household trash.

If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:

• made of a heavy-duty plastic;
• can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out;
• upright and stable during use;
• leak-resistant, and
• properly labeled to warn of hazardous waste inside the container.

When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. Do not reuse or share needles or syringes with another person. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA’s website at:

http://www.fda.gov/safesharpsdisposal

Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. Do not recycle your used sharps disposal container.

Giving your FIASP® injection:

• Inject your FIASP® exactly as your healthcare provider has shown you. Your healthcare provider should tell you if you need to pinch the skin before injecting.
• You should take your dose of FIASP® at the start of a meal or within 20 minutes after starting a meal.
• FIASP® can be injected under the skin (subcutaneously) of your stomach area, upper legs, or upper arms, infused in an insulin pump into an area of your body recommended in the instructions that come with your insulin pump, or given through a needle in your arm (intravenously) by your healthcare provider. Do not inject FIASP® into your muscle.
• If you use FIASP® in an insulin pump, you should change the infusion sets and the infusion set insertion site according
How should I store FIASP®?

• Do not freeze FIASP®. Do not use FIASP® if it has been frozen.
• Keep FIASP® away from excessive heat or light.

All unopened vials:

• Store unopened FIASP® vials in the refrigerator at 36°F to 46°F (2°C to 8°C) or at room temperature below 86°F (30°C).
• If unopened vials have been stored in the refrigerator, vials may be used until the expiration date printed on the label.
• If unopened vials have been stored at room temperature, vials should be thrown away after 28 days.

After vials have been opened:

• Opened FIASP® vials can be stored in the refrigerator at 36°F to 46°F (2°C to 8°C) or at room temperature below 86°F (30°C).
• Throw away all opened FIASP® vials after 28 days (including 6 days pump in-use time), even if they still have insulin left in them.

General information about the safe and effective use of FIASP®:

• Always use a new syringe and needle for each injection to help ensure sterility and prevent blocked needles.
• Do not reuse or share syringes or needles with other people. You may give other people a serious infection or get a serious infection from them.
• Keep FIASP® vials, syringes, and needles out of the reach of children.

This Instructions for Use has been approved by the U.S. Food and Drug Administration.
Instructions for Use

FIASP® (leu'asp) PenFill® 3 mL cartridge 100 Units/mL (U-100) (insulin aspart injection)

• Do not share your PenFill® cartridge or PenFill® cartridge compatible insulin delivery device with other people, even if the needle has been changed. You may give other people a serious infection, or get a serious infection from them.

• Your healthcare provider should show you or your caregiver how to inject FIASP® the right way before you inject it for the first time.

• FIASP® PenFill® cartridge 100 Units/mL is a prefilled single-patient-use cartridge containing 300 units of U-100 FIASP® (insulin aspart injection).

• After you insert the PenFill® cartridge in your device, you can use it for multiple injections. Read the instruction manual that comes with your insulin delivery device for complete instructions on how to use the PenFill® cartridge with the device.

• This PenFill® cartridge is not recommended for use by the blind or visually impaired without the assistance of a person trained in the proper use of the product and your insulin delivery device.

• If using a new FIASP® PenFill® cartridge, start with Step 1.

• If the FIASP® PenFill® cartridge has already been used, start with Step 2.

Supplies you will need to give your FIASP® injection:

• FIASP® PenFill® cartridge

• Novo Nordisk 3 mL PenFill® cartridge compatible insulin delivery device

• 1 new NovoFine®, NovoFine® Plus, or NovoTwist® needle

• Alcohol swab

• Adhesive bandage

• Cotton gauze

• A sharps container for throwing away used PenFill® cartridges and needles. See “After your injection” at the end of these instructions.

How to use the FIASP® PenFill® cartridge

• Wash your hands with soap and water.

• Before you start to prepare your injection, check the FIASP® PenFill® cartridge label to make sure that it contains the insulin you need. This is especially important if you take more than 1 type of insulin.

• The tamper-resistant foil should be in place before the first use. If the foil has been broken or removed before your first use of the cartridge, do not use it. Call Novo Nordisk at 1-800-727-6500.

• Carefully look at the cartridge and the insulin inside it. Check that the FIASP® cartridge:
  • is not damaged, for example cracked or leaking
  • is not loose on the threaded end

• FIASP® should look clear and colorless. Do not use FIASP® if it is cloudy or colored or if the threaded end is loose (See Figure B).

Step 1:

• Insert a 3 mL cartridge with the threaded end first into your Novo Nordisk 3 mL PenFill® cartridge compatible insulin delivery device (See Figure C).

• If you drop your device, check the insulin cartridge for damage such as cracks or leaking. If your cartridge is damaged, throw it away and use a new one.

Prepare your device with a new needle

Step 2:

• Take a new needle, and tear off the paper tab. Always use a new needle for each injection to make sure the needle is free of germs (sterile) and to prevent blocked needles. Do not attach a new needle to your device until you are ready to give your injection. Do not reuse or share your needles with other people. You may give others a serious infection, or get a serious infection from them.

• Be careful not to bend or damage the needle before you use it.

• Push the needle straight onto the device. Turn the dose selector clockwise until it is on tight (See Figure D).

• Pull off the outer needle cap (See Figure E). Do not throw it away. You will need it after the injection to safely remove the needle.

• Pull off the inner needle cap and throw it away (See Figure F). Do not try to put the inner needle cap back on the needle.

Check to make sure that the dose counter is set to 0. (See Figure H). The pointer should line up with your dose. When turning the dose selector, be careful to press the dose button as insulin will come out. You will hear a click for every single unit dialed. Do not set the dose by counting the number of clicks you hear because you may get an incorrect dose.

• Refer to your insulin delivery device manual if necessary.

Inject your dose

Step 7:

• Do the injection exactly as shown to you by your healthcare provider. Your healthcare provider should tell you if you need to pinch the skin before injecting.

• You should take your dose of FIASP® at the start of a meal or within 20 minutes after starting a meal.

• FIASP® can be injected under the skin (subcutaneously) of your stomach area (abdomen), upper legs (thighs), or upper arms (See Figure I).

• Change (rotate) your injection sites within the area you choose for each dose to reduce your risk of getting lipodystrophy (pits in skin or thickened skin) and localized cutaneous amyloidosis (skin with lumps) at the injection sites.

• Do not use the same injection site for each injection. Do not inject where the skin has pits, is thickened, or has lumps. Do not inject where the skin is tender, bruised, scaly or hard, or into scars or damaged skin.

• Clean your injection site with an alcohol swab. Let your skin dry. Do not touch this area again before injecting.

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

Check the insulin flow

Step 5:

• Small amounts of air may collect in the cartridge during normal use. You must do an airshot before each injection to avoid injecting air and to make sure you receive the prescribed dose of your medicine.

• Do the airshot as described in the instruction manual that comes with your device.

• Keep testing your Novo Nordisk 3 mL PenFill® cartridge compatible insulin delivery device until you see insulin at the needle tip. If you still do not see a drop of insulin after 6 times, change the needle and repeat this step. This makes sure that any air bubbles are removed and that insulin is getting through the needle (See Figure G).

Select your dose

Step 6:

• Check to make sure that the dose counter is set to 0.

• Turn the dose selector clockwise to select the dose you need to inject (See Figure H). The pointer should line up with your dose. When turning the dose selector, be careful not to press the dose button as insulin will come out. You will hear a click for every single unit dialed. Do not set the dose by counting the number of clicks you hear because you may get an incorrect dose.

• Refer to your insulin delivery device manual if necessary.

Step 3:

• Pull off the outer needle cap (See Figure E). Do not throw it away. You will need it after the injection to safely remove the needle.

• Pull off the inner needle cap and throw it away (See Figure F). Do not try to put the inner needle cap back on the needle.

Step 4:

Step 8:

• You should take your dose of FIASP® at the start of a meal or within 20 minutes after starting a meal.

• FIASP® can be injected under the skin (subcutaneously) of your stomach area (abdomen), upper legs (thighs), or upper arms (See Figure I).

• Change (rotate) your injection sites within the area you choose for each dose to reduce your risk of getting lipodystrophy (pits in skin or thickened skin) and localized cutaneous amyloidosis (skin with lumps) at the injection sites.

• Do not use the same injection site for each injection. Do not inject where the skin has pits, is thickened, or has lumps. Do not inject where the skin is tender, bruised, scaly or hard, or into scars or damaged skin.

• Clean your injection site with an alcohol swab. Let your skin dry. Do not touch this area again before injecting.
• Insert the needle into your skin. Press and hold down the dose button until the dose counter shows “0”. Continue to keep the dose button pressed and keep the needle in your skin and slowly count to 6 (see Figure J).

• Remove the needle from your skin.

You may see a drop of FIASP® at the needle tip after injecting. This is normal and has no effect on the dose you just received. If blood appears after you take the needle out of your skin, press the injection site lightly with a cotton gauze and cover with an adhesive bandage, if necessary. Do not rub the area.

After your injection

Step 8:

• Lay your outer needle cap on a flat surface. Carefully, lead the needle tip into the outer needle cap without touching the needle (See Figure K) and push the outer needle cap completely on.

• Hold the black cartridge holder on the insulin delivery device and unscrew the needle counterclockwise (See Figure L).

• Throw away (dispose of) the needle in an FDA-cleared sharps container as your healthcare professional has instructed you.

• Put your empty FIASP® PenFill® cartridge and used needles in a FDA-cleared sharps disposal container right away after use. Do not throw away (dispose of) loose needles and PenFill® cartridges in your household trash.

• If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
  - made of a heavy-duty plastic
  - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out
  - upright and stable during use
  - leak-resistant
  - properly labeled to warn of hazardous waste inside the container

• When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. Do not reuse or share your needles or syringes with other people. For more information about the safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA’s website at: http://www.fda.gov/safesharpsdisposal.

• Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. Do not recycle your used sharps disposal container.

Step 9:

• Keep the 3 mL PenFill® cartridge in the device. Do not store your device with a needle attached. This will prevent infection or leakage of insulin and will make sure that you receive the right dose of FIASP®.

• Put the pen cap on your device after each use to protect the insulin from light (See Figure M).

How should I store my FIASP® PenFill® cartridge?

Before use:

• Store unused FIASP® PenFill® cartridges in the refrigerator at 36°F to 46°F (2°C to 8°C).

• Do not freeze FIASP®. Do not use FIASP® if it has been frozen.

• Unused PenFill® cartridges may be used until the expiration date printed on the label, if kept in the refrigerator.

• If FIASP® is stored mistakenly outside of refrigeration between 47°F (9°C) to 86°F (30°C) prior to first use, it should be used within 28 days or thrown away.

PenFill® cartridges in use:

• Store the PenFill® cartridge you are currently using in the insulin delivery device at room temperature below 86°F (30°C) for up to 28 days. Do not refrigerate.

• Keep FIASP® away from heat or light.

• The FIASP® PenFill® cartridge you are using should be thrown away after 28 days, even if it still has insulin left in it.

General Information about the safe and effective use of FIASP®.

• Keep FIASP® PenFill® cartridges and needles out of the reach of children.

• Do not share FIASP® PenFill® cartridges or needles with other people. You may give other people a serious infection, or get a serious infection from them.

• Always carry extra insulin of the same type(s) you use in case of loss or damage.

This Instructions for Use has been approved by the U.S. Food and Drug Administration.