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----------
Indications and Usage (1) ----------12/2019
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 adult and pediatric patients 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):*
  - Inject at the start of a meal or within 20 minutes after starting a meal into the abdomen, upper arm, or thigh.
  - Rotate injection sites within the same region to reduce the risk of lipodystrophy and localized cutaneous amyloidosis.
  - Should generally be used in regimens with an intermediate- or long-acting insulin.
- *Continuous Subcutaneous Infusion (Insulin Pump) (2.2):*
  - 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.
  - 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----------
- During episodes of hypoglycemia (4).
- Hypersensitivity to insulin aspart or one of the excipients in FIASP (4).

----------WARNINGS AND PRECAUTIONS----------
- *Never share* a FIASP FlexTouch pen, PenFill cartridge or PenFill cartridge device between patients, even if the needle is changed (5.1).
- *Hyperglycemia 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 frequeny 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 Ketoacidosis 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/infusion 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 Increase Hypoglycemia Risk or Increase or Decrease Blood Glucose Lowering Effect:* Adjustment of dosage may be needed; closely monitor blood glucose (7).
- *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: 12/2019

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

FIASP is indicated to improve glycemic control in adult and pediatric patients with diabetes mellitus.

2 DOSAGE 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 resume 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 system's 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)]*.
- Train patients using continuous subcutaneous insulin 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 sets and the infusion set insertion site according to the manufacturers user manual.
- Do not mix with other insulins or diluents in the insulin pump .
- Do not expose FIASP in the pump reservoir to 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 hypoglycemia 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 patterns (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 as 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 delivery device

4 CONTRAINDICATIONS

FIASP is contraindicated

- During episodes of hypoglycemia *[see Warnings and Precautions (5.3)]*.
- 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 Hyperglycemia or Hypoglycemia with Changes in Insulin Regimen

Changes in an insulin regimen (e.g., insulin strength, manufacturer, type, injection site or method of administration) may affect 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 anti-diabetic treatment may be needed.

5.3 Hypoglycemia

Hypoglycemia is the most common adverse reaction of all insulin therapies, including FIASP *[see Adverse Reactions (6.1)]*. Severe hypoglycemia can cause seizures, may lead to unconsciousness, may be life-threatening, or cause death. Hypoglycemia 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 hypoglycemia *[see Contraindications (4)]*.

Hypoglycemia can happen suddenly and symptoms may differ in each individual and change over time in the same individual. Symptomatic awareness of hypoglycemia 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 hypoglycemia.

Risk Factors for Hypoglycemia

The risk of hypoglycemia 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 hypoglycemia usually reflects the time-action profile of the administered insulin formulation. As with all insulin preparations, the glucose lowering effect time course 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 Use in Specific Populations (8.4), Clinical Pharmacology (12.2)]*.

Other factors which may increase the risk of hypoglycemia include changes in meal pattern (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 hypoglycemia *[see Use in Specific Populations (8.6, 8.7)]*.

Risk Mitigation Strategies for Hypoglycemia

Patients and caregivers must be educated to recognize and manage hypoglycemia. Self-monitoring of blood glucose plays an essential role in the prevention and management of hypoglycemia. In patients at higher risk for hypoglycemia and patients who have reduced symptomatic awareness of hypoglycemia, increased frequency of blood glucose monitoring is recommended.

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 in patients at risk for hypokalemia if indicated (e.g., patients using potassium-lowering medications, patients taking medications sensitive to potassium concentrations).

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)]*. If hypersensitivity reactions occur, discontinue FIASP; treat per standard of care and monitor until symptoms and signs resolve. FIASP is contraindicated in patients who have had 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 ketoacidosis. 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 pump therapy 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 adult patients with type 1 diabetes to FIASP in one clinical trial with a mean exposure duration of 25 weeks *[see Clinical Studies (14.2)]*. 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 and 7% were Hispanic. The mean BMI was 26.7 kg/m^2 and the mean HbA_{1c} at baseline was 7.6%.

The data in Table 2 reflect the exposure of 341 adult 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/m^2 and the mean HbA_{1c} at baseline was 8.0%.

The data in Table 3 reflect the exposure of 519 pediatric patients with type 1 diabetes to FIASP in one clinical trial with a mean exposure duration of 26 weeks *[see Clinical Studies (14.3)]*. The mean age was 11.7 years and the mean duration of diabetes was 4.4 years. 54% were male, 81% were Caucasian, 16% were Asian and 2% were Black or African American. The mean BMI was 19.7 kg/m^2 and the mean HbA_{1c} at baseline was 7.6%.

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 Adult Patients with Type 1 Diabetes

	Mealtime FIASP + Insulin detemir (N=386)	**Postmeal FIASP + Insulin detemir (N=377)**
Nasopharyngitis	20.2	23.9
Upper respiratory tract infection	9.1	7.4
Nausea	4.9	5.0
Diarrhea	5.4	3.2
Back pain	5.2	4.0

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

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

	FIASP + Insulin glargine (N=341)
Urinary tract infection	5.9

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

Table 3: Adverse Reactions (%*) in Pediatric Patients with Type 1 Diabetes

	Mealtime FIASP + Insulin degludec (N=261)	**Postmeal FIASP + Insulin degludec (N=258)**
Viral upper respiratory tract infection	23.0	20.5
Upper respiratory tract infection	8.4	12.4
Influenza	7.7	5.8
Rhinitis	3.8	6.2
Headache	6.1	10.1
Pyrexia	8.4	6.2
Vomiting	3.4	8.1

*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 and pediatric patients with type 1 diabetes treated with FIASP in clinical trials are shown in Table 4 *[see Clinical Studies (14)]*.

Table 4. Proportion (%) of Patients with Type 1 Diabetes and Type 2 Diabetes Experiencing at Least One Episode of Severe Hypoglycemia in Adult and Pediatric Clinical Trials

	Study A (Type 1) Adults		**Study B (Type 2) Adults**	**Study E (Type 1) Pediatric**		**Study D (Type 1 CSII)**
	Mealtime FIASP + Insulin detemir (N=386)	**Postmeal FIASP + Insulin detemir (N=377)**	**FIASP + Insulin glargine (N=341)**	**Mealtime FIASP + Insulin degludec (N=261)**	**Postmeal FIASP + Insulin degludec (N=258)**	**FIASP (N=236)**
Severe hypoglycemia*	6.7	8.0	3.2	1.1	3.1	4.7

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

Blood glucose confirmed hypoglycemia was defined as a self-measured glucose calibrated to plasma of less than 56 mg/dL.

In Study D, adult patients with type 1 diabetes treated with FIASP in a pump reported a higher rate of blood glucose confirmed hypoglycemic episodes within the first hour after a meal compared to patients treated with NovoLog *[see Clinical Trials (14.5)]*.

In Study E, pediatric patients with type 1 diabetes treated with mealtime and postmeal FIASP reported a higher rate of blood glucose confirmed hypoglycemic episodes compared to patients treated with NovoLog; the imbalance was greater during the nocturnal period *[see Use in Specific Populations (8.4), Clinical Trials (14.3)]*.

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 adult patients treated with FIASP. Allergic skin manifestations reported with FIASP in 1.7% of adult patients from the clinical program include eczema, rash, rash pruritic, urticaria and dermatitis. In Study D, allergic reactions were reported in 4.2% of adult patients with type 1 diabetes treated with FIASP. In Study E, allergic reactions were reported in 4% of pediatric patients with type 1 diabetes treated with Fiasp.

Lipodystrophy

Administration of insulin, including FIASP, has resulted in lipohypertrophy (enlargement or thickening of tissue) and lipoatrophy (depression in the skin). In the clinical program, lipodystrophy was reported in 0.4% of adult patients and 2.1% of pediatric 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 to a few weeks, but in some occasions, may require discontinuation of FIASP. In the clinical program, injection site reactions occurred in 1.6% of adult patients treated with FIASP. In Study A, adult 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 adult patients with type 1 diabetes treated with FIASP. In Study E, injection site reactions were reported in 4.2% of pediatric 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 decrease in glucosuria. In Study A, adult patients with type 1 diabetes treated with FIASP gained an average of 0.7 kg and in Study B, adult 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 0.8% of adult patients treated with FIASP.

6.2 Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity. 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 in the studies described below with the incidence of antibodies in other studies or to other insulin products may be misleading.

In a 26-week study in adult subjects with type 1 diabetes (Study A *[see Clinical Studies (14.2)]*), among the 763 subjects who received FIASP, 97.2% were positive for cross-reacting anti-insulin 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.

In a 26-week study in pediatric subjects with type 1 diabetes (Study E *[see Clinical Studies (14.3)]*), among the 519 subjects who received FIASP, 97.1% were positive for cross-reacting anti-insulin antibodies (AIA) at least once during the study, including 94.6% that were positive at baseline. A total of 19.1% of patients who received FIASP were positive for anti-drug (insulin aspart) antibodies (ADA) at least once during the study, including 16.0% 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. Hyperglycemia has been reported with repeated insulin injections into areas of localized cutaneous amyloidosis; hypoglycemia has been reported with a sudden change to an unaffected injection site.

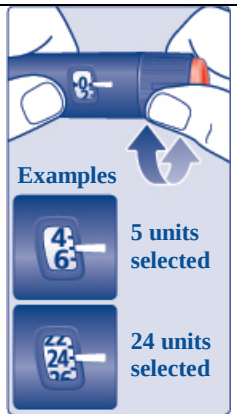
7 DRUG INTERACTIONS

Table 5 includes clinically significant drug interactions with FIASP.

Table 5. Clinically Significant Drug Interactions with FIASP

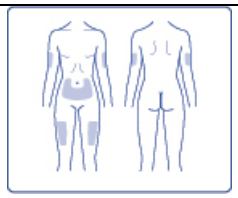
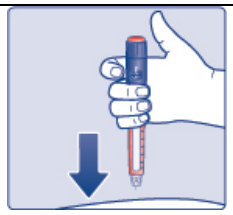
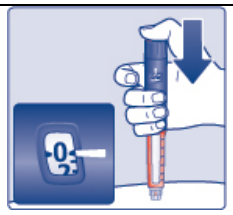
Drugs That May Increase the Risk of Hypoglycemia	
Drugs:	Antidiabetic agents, ACE inhibitors, angiotensin II receptor blocking agents, disopyramide, fibrates, fluoxetine, monoamine oxidase inhibitors, pentoxifylline, pramlintide, salicylates, somatostatin analogs (e.g., octreotide), and sulfonamide antibiotics.
Intervention:	Dose reductions and increased frequency of glucose monitoring may be required when FIASP is co-administered with these

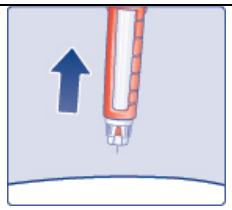
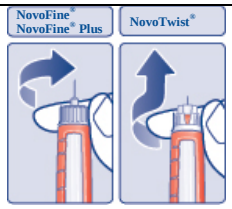
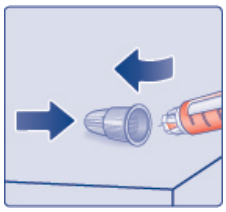
Selecting your dose:

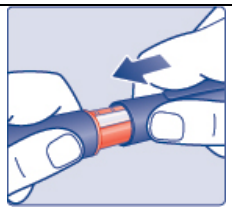
Step 10: **Check to make sure the dose selector is set at 0.** **Turn the dose selector to select the number of units you need to inject.** The dose pointer should line up with your dose (See Figure K). o If you select the wrong dose, you can turn the dose selector forwards or backwards to the correct dose. o The **even** numbers are printed on the dial. o The **odd** numbers are shown as lines.	 (Figure K)
The FIASP FlexTouch Pen insulin scale will show you how much insulin is left in your Pen (See Figure L).	 (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).	 (Figure M)
Step 12: • **Insert the needle into your skin** (See Figure N). o **Make sure you can see the dose counter. Do not** cover it with your fingers; this can stop your injection.	 (Figure N)
Step 13: • **Press and hold down the dose button until the dose counter shows "0"** (See Figure O). 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). o **When the dose counter returns to "0", you will not**	 (Figure O)

get your full dose until 6 seconds later. o **If the needle is removed before you count to 6, you may see a stream of insulin coming from the needle tip.** o **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.**	 (Figure P)
Step 14: • **Pull the needle out of your skin** (See Figure Q). o 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.	 (Figure Q)
Step 15: • **Carefully remove the needle from the Pen and throw it away** (See Figure R). o **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. o **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.	 (Figure R)  (Figure S)

Step 16: • Replace the Pen cap by pushing it straight on (See Figure T).	 (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

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For more information go to
www.FIASPflextouch.com