Insulin Aspart Injection

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

Insulin Aspart Injection, for subcutaneous or intravenous use

Initial U.S. Approval: 2000

——— RECENT MAJOR CHANGES ———

Dosage and Administration (2.1) 12/2018
Dosage and Administration (2.2) 11/2019
Warnings and Precautions (5.2) 11/2019

——— INDICATIONS AND USAGE ———

• Insulin aspart is rapid acting human insulin analog indicated to improve glycemic control in adults and children with diabetes mellitus (1).

——— DOSAGE AND ADMINISTRATION ———

• See Full Prescribing Information for important administration and dosage instructions (2.1, 2.2, 2.3, 2.4, 2.5).

Subcutaneous injection (2.2):

• Inject subcutaneously within 5-10 minutes before a meal into the abdominal area, thigh, buttocks or upper arm.
• Rotate injection sites within the same region from one injection to the next to reduce risk of lipodystrophy and localized cutaneous amyloidosis.
• Should generally be used in regimens with an intermediate- or long-acting insulin.

Continuous Subcutaneous Insulin Infusion (Insulin Pump) (2.2):

• Administer by continuous subcutaneous infusion using an insulin pump in a region recommended in the instructions from the pump manufacturer.
• Rotate the injection sites within the same region from one injection to the next to reduce the risk of lipodystrophy and localized cutaneous amyloidosis.
• Change the Insulin aspart in the reservoir at least every 6 days.
• Change the infusion set and the infusion set insertion site at least every 3 days.
• Do not mix with other insulins or diluents in the pump.

Intravenous Administration (2.2):

• Dilute insulin aspart to concentrations from 0.05 unit/mL to 1 unit/mL insulin aspart in infusion systems using polypropylene infusion bags.

• Insulin aspart is stable in infusion fluids such as 0.9% sodium chloride.
• Individualize and adjust the dosage of insulin aspart based on route of administration, the individual's metabolic needs, blood glucose monitoring results and glycemic control goal (2.4).
• Dosage adjustments may be needed with changes in physical activity, changes in meal patterns (i.e., macronutrient content or timing of food intake), changes in renal or hepatic function or during acute illness (2.4).

——— DOSAGE FORMS AND STRENGTHS ———

Each presentation contains 100 Units of insulin aspart per mL (U-100).

• 10 mL multiple-dose vial (3)
• 3 mL single-patient-use PenFill® cartridges for the 3 mL PenFill® cartridge device (3)
• 3 mL single-patient-use Insulin Aspart FlexPen® (3)

——— CONTRAINDICATIONS ———

• During episodes of hypoglycemia (4).
• Hypersensitivity to insulin aspart or one of its excipients.

——— WARNINGS AND PRECAUTIONS ———

• Never share an Insulin Aspart FlexPen®, PenFill® cartridge or FlexPen® 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 or hepatic impairments and hypoglycemia unawareness (5.3).
• Medication Errors: Accidental mix-ups between insulin products can occur. Instruct patients to check insulin labels before injection (5.4).
• Hypersensitivity reactions: Severe, life-threatening, generalized allergy, including anaphylaxis, may occur. Discontinue insulin aspart, treat, and monitor, if indicated (5.5).
• Hypokalemia: May be life-threatening. Monitor potassium levels in patients at risk of hypokalemia and treat if indicated (5.6).

——— ADVERSE REACTIONS ———

Adverse reactions observed with insulin aspart include: hypoglycemia, allergic reactions, local injection site reactions, lipodystrophy, rash, and pruritus (6).

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

——— DRUG INTERACTIONS ———

• Drugs that may increase the risk of hypoglycemia: anti-diabetic agents, ACE inhibitors, angiotensin II receptor blocking agents, disopyramide, fentanyl, fluoxetine, monoamine oxidase inhibitors, pentoxifylline, pramlintide, propoxyphene, salicylates, somatostatin analog (e.g., octreotide), and sulfonamide antibiotics (7).
• Drugs that may decrease the blood glucose lowering effect: atypical antipsychotics, corticosteroids, diazoxide, diuretics, estrogens, glucagon, insulin, lactulose, niacin, oral contraceptives, phenothiazines, progestogens (e.g., in oral contraceptives), protease inhibitors, somatropin, sympathomimetic agents (e.g., albuterol, epinephrine, terbutaline), and thyroid hormones (7).
• Drugs that may increase or decrease the blood glucose lowering effect: alcohol, beta-blockers, clonidine, lithium salts, and pentamidine (7).
• Drugs that may blunt the signs and symptoms of hypoglycemia: beta-blockers, clonidine, guanethidine, and reserpine (7).

——— USE IN SPECIFIC POPULATIONS ———

• Pediatric: Has not been studied in children with type 2 diabetes. Has not been studied in children with type 1 diabetes <2 years of age (6.4).

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

Revised: 11/2019
FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE
Insulin aspart is a rapid-acting human insulin analog intended to improve glycemic control in adult and children with diabetes mellitus.

2 DOSAGE AND ADMINISTRATION

2.1 Important Administration Instructions
• Always check insulin labels before administration [see Warnings and Precautions (5.4)].
• Inspect insulin aspart visually before use. It should appear clear and colorless. Do not use insulin aspart if particulate matter or coloration is noted.
• Use Insulin Aspart FlexPen® with caution in patients with visual impairment who may rely on audible clicks to dial their dose.
• Use PenFill® cartridges with caution in patients with visual impairment.
• Do NOT mix insulin aspart with other insulins when administering using a continuous subcutaneous infusion pump.

2.2 Route of Administration
Subcutaneous Injection
• Inject insulin aspart subcutaneously within 5-10 minutes before a meal into the abdominal area, thigh, buttocks or upper arm.
• 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 Warnings and Precautions (5.2) and Adverse Reactions (6.1, 6.3)].
• During changes to a patient’s insulin regimen, increase the frequency of blood glucose monitoring [see Warnings and Precautions (5.2)].
• The Insulin Aspart FlexPen® dial in 1-unit increments.
• Administer insulin aspart by subcutaneous injection in a region recommended in the instructions from the pump manufacturer. Rotate injection sites within the same region to reduce the risk of lipodystrophy or localized cutaneous amyloidosis [see Warnings and Precautions (5.2) and Adverse Reactions (6.1, 6.3)].
• During changes to a patient’s insulin regimen, increase the frequency of blood glucose monitoring [see Warnings and Precautions (5.2)].
• Check for accessibility in patients who have visual impairment who may rely on audible clicks to dial their dose.
• Change the insulin aspart in the reservoir at least every 6 days. Follow the instructions from the pump manufacturer. If the insulin aspart in the reservoir is used more frequently, the concentration of insulin aspart in the reservoir may be less than expected.
• Change the infusion set and the infusion set insertion site at least every 3 days.
• Do NOT dilute or mix insulin aspart when administering by continuous subcutaneous infusion.
• Do NOT expose insulin aspart in the pump reservoir to temperatures greater than 70°F (21°C).

Intravenous Administration
• Dilute insulin aspart to concentrations from 0.05 unit/mL to 1 unit/mL. This is the only concentration of insulin aspart suitable for IV administration. Insulin aspart is stable in infusion fluids such as 0.9% sodium chloride.
• Administer insulin aspart 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, 5.6) and How Supplied/Storage and Handling (16.2)].

2.3 Dosage Information

Individualize and adjust the dosage of insulin aspart based on the rate of administration, the individual’s metabolic needs, blood glucose monitoring results, and results of glucose monitoring.

Dosage adjustments may be needed with changes in physical activity, changes in meal patterns (i.e., macronutrient content or timing of food intake), changes in renal or hepatic function or during acute illness [see Warnings and Precautions (5.2, 5.3) and Use in Specific Populations (8.6, 8.7)].

Dosage adjustment may be needed when switching from another insulin to insulin aspart [see Warnings and Precautions (5.2)].

2.4 Dosage Adjustment Due to Drug Interactions
Dosage adjustment may be needed when insulin aspart is coadministered with certain drugs [see Drug Interactions (7)].

2.5 Instructions for Mixing with Other Insulins
Insulin aspart may be mixed with NPH insulin preparations ONLY:
• If insulin aspart is mixed with NPH insulin, draw insulin aspart into the syringe first and inject immediately before mixing.

Insulin aspart continuous subcutaneous infusion route (Insulin Pump)

3 DOSAGE FORMS AND STRENGTHS
Insulin aspart 100 units per mL (U-100) is available as a clear and colorless solution for injection in:
• 10 mL multiple-dose vial
• 5 mL single-use PenFill® cartridges for the 3 mL PenFill® cartridge delivery device with NovoFine® disposable needles
• 3 mL single-use Insulin Aspart FlexPen®

4 CONTRAINDICATIONS
Insulin aspart is contraindicated:
• During episodes of hypoglycemia [see Warnings and Precautions (5.3)].
• In patients with hypersensitivity to insulin aspart or one of its excipients [see Warnings and Precautions (5.3)].

5 WARNINGS AND PRECAUTIONS

5.1 Never Share an Insulin Aspart FlexPen®, PenFill® Cartridge, or PenFill® Cartridge Device Between Patients
Insulin Aspart FlexPen®, PenFill® cartridge, and PenFill® cartridge devices should never be shared between patients, even if the needle is changed. Patients using insulin aspart vials must 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 and 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 hypoglycemia and, in a sudden change in the injection site (to an unaffected area) has been reported to result in hyperglycemia [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 hyperglycemia. For patients with type 2 diabetes, dosage adjustments of concomitant anti-diabetic medications may be required.

5.3 Hypoglycemia
Hypoglycemia is the most common adverse effect of all insulin therapies, including insulin aspart. 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). 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 renal or hepatic impairment who may rely on audible clicks to dial their dose. Patients with renal or hepatic impairment may be at higher risk of hypoglycemia and patients who have reduced symptomatic awareness of hypoglycemia may be at higher risk of hypoglycemia. Hypoglycemia is the most common adverse effect of all insulin therapies. Patients and caregivers must be educated to recognize and manage hypoglycemia.

5.4 Hypoglycemia Due to Medication Errors
Accidental mix-ups between insulin aspart and other insulin products have been reported. To avoid medication errors between insulin aspart and other insulins, instruct patients to always check the insulin label before each injection.

5.5 Hypersensitivity and Allergic Reactions
Severe, life-threatening, generalized allergic, including anaphylaxis, can occur with insulin products, including insulin aspart. If hypersensitivity reactions occur, discontinue insulin aspart treatment per standard of care and monitor until symptoms and signs resolve [see Adverse Reactions (6)].

Insulin aspart is contraindicated in patients who have had hypersensitivity reactions to insulin aspart or one of the excipients [see Contraindications (4)].

5.6 Hypokalemia
All insulin products, including insulin aspart, 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 serum potassium concentration).

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 insulin aspart, 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 Ketosis Due to Insulin Pump Device Malfunction
Device malfunction of the insulin pump or infusion set or insulin degradation can rapidly lead to hyperglycemia and ketoacidosis. Prompt identification and correction of the cause of hyperglycemia or ketosis is necessary. Interim subcutaneous injections with insulin aspart may be required. Patients using continuous subcutaneous infusion pump therapy must be trained to administer insulin by injection and have alternate insulin therapy available in case of pump failure [see 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)].
• Hypersensitivity and allergic reactions [see Warnings and Precautions (5.5)].
• Hypokalemia [see Warnings and Precautions (5.6)].

6.1 Clinical Trial Experience
Because clinical trials are conducted under widely varying designs, the adverse reaction rates reported in one clinical trial may not be easily compared to those rates reported in another clinical trial, and may not reflect the rates actually observed in clinical practice. The safety of insulin aspart was evaluated in two treat-to-target trials of 6 months duration, conducted in subjects with type 1 diabetes or type 2 diabetes [see Clinical Studies (14)].

The data in Table 1 reflect the exposure of 596 patients with type 1 diabetes to insulin aspart in one clinical trial with a mean exposure duration to insulin aspart of 24 weeks. The mean age was 38.9 years. Fifty-one percent were male, 94% were Caucasian, 2% were Black and 4% were other races. The mean body mass index (BMI) was 26.5 kg/m². The mean duration of diabetes was 15.7 years and the mean HbA1c at baseline was 7.9%.

The data in Table 2 reflect the exposure of 91 patients with type 2 diabetes to insulin aspart in one clinical trial with a mean exposure duration to insulin aspart of 24 weeks. The mean age was 56.6 years. Sixty-three percent were male, 76% were Caucasian, 9% were Black and 15% were other races. The mean BMI was 42.8 kg/m². The mean duration of diabetes was 12.7 years and the mean HbA1c at baseline was 8.1%.

Common adverse reactions were defined as events occurring in ≥5%, excluding hypoglycemia, of the population studied. Common adverse events occurring at the same rate or greater for insulin aspart-treated subjects than in comparator-treated subjects during clinical trials in patients with type 1 diabetes mellitus and type 2 diabetes mellitus (other than hypoglycemia) are listed in Tables 2 and 3.

Table 1: Adverse reactions occurring in ≥5% of Type 1 Diabetes Mellitus Adult Patients treated with insulin aspart and at the same rate or greater on insulin aspart than on comparator

<table>
<thead>
<tr>
<th>Event</th>
<th>Type 1 Diabetes Mellitus (≥5%)</th>
<th>Comparator (≥5%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>Injury accidental</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>Nausea</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>
insulin aspart + NPH (%)(n=91) Human Regular Insulin + NPH (%)(n=71)

| Hypertension | 11 | 0 |
| Glaucoma | 10 | 5 |
| Sensory disturbance | 9 | 7 |
| Urinary tract infection | 8 | 7 |
| Chest pain | 5 | 3 |
| Headache | 5 | 3 |
| Skin disorder | 2 | 2 |
| Abdominal pain | 5 | 1 |
| Sinusitis | 5 | 1 |

Severe hypoglycemia

Hypoglycemia is the most commonly observed adverse reaction in patients using insulin, including insulin aspart [see Warnings and Precautions (5.3)]. 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 insulin aspart with the incidence of hypoglycemia for other products may be misleading and is not representative of hypoglycemia that will occur in clinical practice.

Severe hypoglycemia was defined as hypoglycemia associated with central nervous system symptoms and requiring the intervention of another person or hospitalization.

The incidence of severe hypoglycemia in adult and pediatric patients receiving subcutaneous insulin aspart with type 1 diabetes mellitus was 17% in 24 weeks and 6% in 24 weeks, respectively [see Clinical Studies (6.2)].

The incidence of severe hypoglycemia in adult patients receiving subcutaneous insulin aspart with type 2 diabetes mellitus was 10% at 24 weeks.

The incidence of severe hypoglycemia in adult and pediatric patients with type 1 diabetes mellitus receiving insulin aspart via continuous subcutaneous insulin infusion by external pump was 2% at 16 weeks and 10% at 16 weeks respectively.

No severe hypoglycemic episodes were reported in adult patients with type 2 diabetes mellitus receiving insulin aspart via continuous subcutaneous insulin infusion by external pump at 16 weeks.

Allergic Reactions

Some patients taking insulin therapy, including insulin aspart have experienced erythema, local edema, and pruritus at the site of injection.

These conditions were usually self-limiting. Severe cases of generalized allergy (anaphylaxis) have been reported [see Warnings and Precautions (5.5)].

Insulin injection and glucose control intensification

Intensification or rapid improvement in glucose control has been associated with an increased risk of hypoglycemia, reversible orthostatic hypotension, disorders of gastrointestinal function, retinopathy, and acute painful peripheral neuropathy. However, long-term glycemic control decreases the risk of diabetic retinopathy and neuropathy.

Lipodystrophy

Adipose tissue loss of insulin, including insulin aspart, subcutaneously and via subcutaneous insulin infusion by external pump, has resulted in lipolysis (depression in the skin) or lipohypertrophy (enlargement or thickening of tissue) in some patients [see Dosage and Administration (2.3)].

Peripheral Edema

Insulin products, including insulin aspart, may cause sodium retention and edema, particularly if previously poor metabolic control is improved by intensified insulin therapy.

Weight gain

Weight gain has occurred with some insulin therapies including insulin aspart and has been attributed to the anabolic effects of insulin and the decrease in glucosuria.

6.2 Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to insulin aspart in the studies described below with the incidence of antibodies in other studies or to other products may be misleading.

In a 6-month study with a 6-month extension in adult subjects with type 1 diabetes, 99.3% of patients who received insulin aspart were positive for anti-insulin antibodies (AIA) at least once during the study, including 97.2% that were positive at baseline. A total of 92.1% of patients who received insulin aspart were positive for anti-drug antibodies (ADA) at least once during the study, including 64.8% that were positive at baseline.

In a phase 3 type 1 diabetes clinical trial of insulin aspart, initial increase in titers of antibodies to insulin, followed by a decrease to baseline values, was observed in regular human insulin and insulin aspart treatment groups with similar incidences. These antibodies did not cause deterioration in glycemic control in patients with type 1 diabetes who were receiving insulin aspart with the current dose.

6.3 Post Marketing Experience

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

Medication errors have been reported in which other insulins have been confused with insulin aspart [see Warnings and Precautions (5.4)].

Localized cutaneous amyloidosis at the injection site has occurred with insulin aspart. Hypoglycemia has been reported with delayed insulin injections into areas of localized cutaneous amyloidosis, hypoglycemia has been reported with a sudden change to an unaffected injection site.

7 DRUG INTERACTIONS

Drugs That May Increase the Risk of Hypoglycemia

Drugs: Antidiabetic agents, ACE inhibitors, angiotensin II receptor blockers, disopyramide, fibrates, fluoxetine, monoamine oxidase inhibitors, pentoxifylline, pramlintide, propoxyphene, salicylates, somatostatin analog (e.g., octreotide), and sulfonamide antibiotics.

Intervention: Dose adjustment and increased frequency of glucose monitoring may be required when insulin aspart is co-administered with these drugs.

Drugs That May Decrease the Blood Glucose Lowering Effect of insulin aspart

Drugs: Allopurinol, aminoglycosides, atropine, beta-blockers, chloroquine, cimetidine, clonidine, corticosteroids, diltiazem, digoxin, digitalis, doxorubicin, ergot derivatives, estrogens, fentanyl, haloperidol, heparin, heroin, ketorolac, levodopa, latency, levonorgestrel, lidocaine, lithium, meperidine, metoclopramide, midazolam, mitomycin, monoamine oxidase inhibitors, nonsteroidal anti-inflammatory drugs, opioids, oxcarbazepine, ranitidine, salicylates, somatostatin analog, stilbamidine, theophylline, thiazides, tizanidine, and tretinoin.

Intervention: Side effects can be prevented by diet modification and exercise when indicated, or the drug or insulin aspart may be used with caution under medical supervision.

Drugs That May Increase or Decrease the Blood Glucose Lowering Effect of insulin aspart

Drugs: Alcohol, beta-blockers, clonidine, and lithium salts. Pentamidine may cause hypoglycemia which may be followed by hypoglycemia. Pentamidine may cause hypoglycemia, which may sometimes be followed by hyperglycemia.

Intervention: Dose adjustment and increased frequency of glucose monitoring may be required when insulin aspart is co-administered with these drugs.

Drugs That May blunt Signs and Symptoms of Hypoglycemia

Drugs: Beta-blockers, clonidine, guanethidine and reserpine.

Intervention: Increased frequency of glucose monitoring may be required when insulin aspart is co-administered with these drugs.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Available information from published randomized controlled trials with insulin aspart use during the second trimester of pregnancy have not demonstrated an association with insulin aspart and major birth defects or adverse maternal or fetal outcomes [see Drug Interactions]. 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 unit/kg/day, respectively. Pre- and post-natal development were normal in the offspring of these studies. There were no adverse maternal effects observed in rats at a dose of 50 units/kg/day and in rabbits at a dose of 10 units/kg/day (approximately three times the human subcutaneous dose of 1 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 unit/kg/day for rabbits and equal to the human subcutaneous dose of 1 unit/kg/day for rats, 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 insulin aspart 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 effect of insulin aspart on the breastfed infant. The potential developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for insulin aspart, and any potential adverse effects on the breastfed infant from insulin aspart, or from the underlying maternal condition.

8.4 Pediatric Use

Insulin aspart is approved for use in children for subcutaneous daily injections and for subcutaneous continuous infusion by external insulin pump [see Clinical Studies (14.1, 14.2)]. Insulin aspart has not been studied in pediatric patients younger than 2 years of age. Insulin aspart has not been studied in pediatric patients with type 2 diabetes.

8.5 Geriatric Use

The total number of patients (n=1,375) treated with insulin aspart in 3 controlled clinical studies, 2.6% (n=36) were 65 years of age or over. One-half of these patients had type 1 diabetes (18/365) and one-half had type 2 diabetes (18/30). The HbA1c response to insulin aspart, as compared to regular human insulin, did not differ by age.

8.6 Renal Impairment

Patients with renal impairment may be at increased risk of hypoglycemia and may require more frequent insulin aspart dose adjustment and more frequent 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 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, 5.6)]. Mild 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 neurologic impairment may be treated with intramuscular/subcutaneous glucagon or concentrated intravenous glucose. Sustained hypoglycemia or observation may be necessary because hypoglycemia may recur after apparent clinical recovery. Hypokalemia must be corrected appropriately.

11 DESCRIPTION

Insulin aspart (injection) is a rapid-acting human insulin analog used to lower blood glucose. Insulin aspart is homologous with regular human insulin with the exception of a single substitution of the amino acid proline by aspartic acid in position B28, and is produced by recombinant DNA technology utilizing Saccharomyces cerevisiae (baker’s yeast). Insulin aspart is the empirical formula \( C_{65}H_{110}N_{14}O_{26}S_{2} \) and has a molecular weight of 3,652.

Figure 1. Structural formula of insulin aspart.
Intravenous administration
A double-blind, randomized, two-way crossover study in 16 patients with type 1 diabetes demonstrated that intravenous infusion of insulin aspart resulted in a blood glucose profile that was similar to that after intravenous infusion with regular human insulin. Insulin aspart or human insulin was infused until the patient’s blood glucose decreased to 36 mg/dL or until the patient demonstrated signs of hypoglycemia (rise in heart rate and onset of anxiety), defined as the time of autonomic reaction (R) (see Figure 5).

Mean Blood Glucose (mg/dL)

<table>
<thead>
<tr>
<th>Time (hr)</th>
<th>Insulin Aspart</th>
<th>Regular Human Insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>87.2 ± 12.5</td>
<td>89.1 ± 13.2</td>
</tr>
<tr>
<td>2</td>
<td>85.1 ± 11.9</td>
<td>87.3 ± 12.9</td>
</tr>
<tr>
<td>3</td>
<td>84.3 ± 11.7</td>
<td>86.5 ± 12.6</td>
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<tr>
<td>4</td>
<td>83.5 ± 11.5</td>
<td>85.7 ± 12.5</td>
</tr>
<tr>
<td>5</td>
<td>82.7 ± 11.4</td>
<td>84.9 ± 12.4</td>
</tr>
<tr>
<td>6</td>
<td>82.0 ± 11.3</td>
<td>83.2 ± 11.8</td>
</tr>
</tbody>
</table>

Note: The values are mean ± SD.

12.3 Pharmacokinetics
Subcutaneous administration
Absorption and Bioavailability
In subjects in healthy volunteers (total n=167) and patients with type 1 diabetes (total n=10), the median time to maximum concentration of insulin aspart in these trials was 40 to 50 minutes versus 80 to 120 minutes, for regular human insulin respectively.

The relative bioavailability of insulin aspart (0.15 units/kg) compared to regular human insulin indicates that the two insulins are absorbed to a similar extent.

In a clinical trial in patients with type 1 diabetes, insulin aspart and regular human insulin, both administered subcutaneously at a dose of 0.15 units/kg body weight, reached mean maximum concentrations of 62 and 36 mU/L, respectively.

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

14.2 Clinical Studies in Adult and Pediatric Patients with Type 1 Diabetes and Subcutaneous Daily Injections
Type 1 Diabetes – Adults (see Table 3)
Two 24-week, open-label, active-controlled studies were conducted to compare the safety and efficacy of insulin aspart to regular human insulin injection in 596 type 1 diabetes adults. Because the two study designs and results were similar, data are shown for only one study (see Table 3).

The mean age of the trial population was 38.9 years and mean duration of diabetes was 17.5 years. Fifty-one percent were male. Ninety-four percent were Caucasian, 2% were Black and 4% were Other. The mean BMI was approximately 25.6 kg/m².

Insulin aspart was administered by subcutaneous injection immediately prior to meals and regular human insulin was administered by subcutaneous injection before meals. NPH insulin was administered as the basal insulin in either single or divided daily doses. Changes in HbA1c were comparable for the two treatment regimens in this study (Table 3).

Table 3. Type 1 Diabetes Mellitus – Adults (insulin aspart plus NPH human insulin vs. regular human insulin plus NPH human insulin)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Baseline HbA1c (%)</th>
<th>Treatment Difference in HbA1c (% SD)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin aspart + NPH human insulin (N=906)</td>
<td>Baseline HbA1c (%)</td>
<td>8.3 ± 1.2</td>
<td>8.0 ± 1.2</td>
</tr>
<tr>
<td>Change from Baseline HbA1c (%)</td>
<td>0.3 ± 1.2</td>
<td>0.0 ± 1.0</td>
<td>0.06</td>
</tr>
<tr>
<td>Treatment Difference in HbA1c, Mean (95% confidence interval)</td>
<td>-0.2 (0.3, -0.1)</td>
<td>-0.2 (0.3, -0.1)</td>
<td>0.01</td>
</tr>
<tr>
<td>Values are Mean ± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

14.3 Clinical Studies in Adults with Type 2 Diabetes and Subcutaneous Daily Injections
Type 2 Diabetes – Adults (see Table 4)
One six-month, open-label, active-controlled study was conducted to compare the safety and efficacy of insulin aspart to regular human insulin injection in 596 type 2 diabetes patients with type 2 diabetes (Table 5).

The mean age of the trial population was 56.6 years and mean duration of diabetes was 12.2 years. Sixty-three percent were male. Seventy-six percent were Caucasian, 9% were Black and 15% were Other. The mean BMI was approximately 29.7 kg/m².

Insulin aspart was administered by subcutaneous injection immediately prior to meals and regular human insulin was administered by subcutaneous injection before meals. NPH insulin was similar to the comparative basal insulin in either single or divided daily doses. Changes in HbA1c were comparable for the two treatment regimens.

Table 5. Subcutaneous insulin aspart Administration in Type 2 Diabetes (6 months; n=176)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Baseline HbA1c (%)</th>
<th>Treatment Difference in HbA1c (% SD)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin aspart + NPH human insulin (N=90)</td>
<td>Baseline HbA1c (%)</td>
<td>8.8 ± 1.2</td>
<td>8.4 ± 1.2</td>
</tr>
<tr>
<td>Change from Baseline HbA1c (%)</td>
<td>0.3 ± 1.0</td>
<td>0.0 ± 0.8</td>
<td>0.08</td>
</tr>
<tr>
<td>Treatment Difference in HbA1c, Mean (95% confidence interval)</td>
<td>-0.2 (0.4, 0.01)</td>
<td>-0.2 (0.4, 0.01)</td>
<td>0.01</td>
</tr>
<tr>
<td>Values are Mean ± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

14.4 Pharmacokinetics
The pharmacokinetic and pharmacodynamic properties of insulin aspart given subcutaneously in 18 children 6-12 years of age received an intravenous infusion of either insulin aspart or regular human insulin at 1.5 µL/kg/min for 120 minutes. The mean insulin clearance was similar for the two groups with a geometric mean (95% confidence interval) of 1.2 L/kg/h for insulin aspart and 1.1 L/kg/h for regular human insulin.

After subcutaneous administration in normal male volunteers (n=24), insulin aspart was eliminated with an apparent half-life of 81 minutes.

Figure 4. Serial mean serum free insulin concentration collected up to 6 hours following a single 0.15 units/kg pre-meal dose of insulin aspart (solid curve) or regular human insulin (hatched curve) injected immediately before a meal in 22 patients with type 1 diabetes.

Figure 2. Serial mean serum glucose collected up to 6 hours following a single 0.15 units/kg pre-meal dose of insulin aspart (solid curve) or regular human insulin (hatched curve) injected immediately before a meal in 22 patients with type 1 diabetes.

Intravenous administration
A double-blind, randomized, two-way crossover study in 16 patients with type 1 diabetes demonstrated that intravenous infusion of insulin aspart resulted in a blood glucose profile that was similar to that after intravenous infusion with regular human insulin. Insulin aspart or human insulin was infused until the patient’s blood glucose decreased to 36 mg/dL or until the patient demonstrated signs of hypoglycemia (rise in heart rate and onset of anxiety), defined as the time of autonomic reaction (R) (see Figure 5).

Mean Blood Glucose (mg/dL)

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Insulin Aspart</th>
<th>Regular Human Insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>110 ± 15</td>
<td>112 ± 16</td>
</tr>
<tr>
<td>20</td>
<td>108 ± 14</td>
<td>110 ± 15</td>
</tr>
<tr>
<td>30</td>
<td>106 ± 13</td>
<td>108 ± 14</td>
</tr>
<tr>
<td>40</td>
<td>104 ± 12</td>
<td>106 ± 13</td>
</tr>
<tr>
<td>50</td>
<td>102 ± 11</td>
<td>104 ± 12</td>
</tr>
<tr>
<td>60</td>
<td>100 ± 10</td>
<td>102 ± 11</td>
</tr>
</tbody>
</table>

Note: The values are mean ± SD.
14.4 Clinical Studies in Adults and Pediatrics with Type 1 Diabetes Using Continuous Subcutaneous Insulin Infusion (CSII) by External Pump

Type 1 Diabetes – Adults (see Table 6)

Two open-label, parallel design studies (6 weeks [n=29] and 16 weeks [n=118]) compared insulin aspart to aspart regular human insulin (Velosulin) in adults with type 1 diabetes receiving a subcutaneous infusion with an external insulin pump.

The mean age of the trial population was 42.3 years. Thirty-nine percent were male. Ninety-eight percent were Caucasian and 2% were Black. The two treatment regimens had comparable changes in HbA1c.

Table 6. Adult Insulin Pump Study in Type 1 Diabetes (16 weeks; n=118)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Baseline HbA1c (%)</th>
<th>Mean Change from Baseline HbA1c (%)</th>
<th>Treatment Difference in HbA1c Mean (95% confidence interval)</th>
<th>values are Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin aspart (N=60)</td>
<td>7.3 ± 0.7</td>
<td>0.0 ± 0.2</td>
<td>0.3 (0.0, 0.5)</td>
<td></td>
</tr>
<tr>
<td>Buffered human insulin (N=59)</td>
<td>7.5 ± 0.8</td>
<td>0.2 ± 0.3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are Mean ± SD

Type 1 Diabetes – Pediatric (see Table 7)

A randomized, 16-week, open-label, parallel design study of children and adolescents with type 1 diabetes (n=260) aged 4-18 years compared two subcutaneous infusion regimens administered via an external insulin pump: insulin aspart (n=198) or insulin lispro (n=102). These two treatments resulted in comparable changes from baseline in HbA1c (see Table 7).

14.5 Clinical Studies in Adults with Type 2 Diabetes Using Continuous Subcutaneous Insulin Infusion (CSII) by External Pump

Type 2 Diabetes – Adults (see Table 8)

An open-label, 16-week parallel design trial compared pre-prandial insulin aspart injection in conjunction with NPH injections to insulin aspart administered by continuous subcutaneous infusion in 127 adults with type 2 diabetes.

The mean age of the trial population was 55.1 years. Sixty-four percent were male. Eighty percent were Caucasian, 12% were Black and 8% were Other. The mean BMI was approximately 32.2 kg/m².

The two treatment groups had similar reductions in HbA1c (Table 8).

Table 7. Pediatric Insulin Pump Study in Type 1 Diabetes (16 weeks; n=298)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Baseline HbA1c (%)</th>
<th>Mean Change from Baseline HbA1c (%)</th>
<th>Treatment Difference in HbA1c Mean (95% confidence interval)</th>
<th>values are Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin aspart (N=118)</td>
<td>8.0 ± 0.9</td>
<td>-0.1 ± 0.8</td>
<td>-0.1 (0.3, 0.0)</td>
<td></td>
</tr>
<tr>
<td>Lispro (N=100)</td>
<td>8.2 ± 0.8</td>
<td>-0.1 ± 0.7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are Mean ± SD

Table 8. Pump Therapy in Type 2 Diabetes (16 weeks; n=127)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Baseline HbA1c (%)</th>
<th>Mean Change from Baseline HbA1c (%)</th>
<th>Treatment Difference in HbA1c Mean (95% confidence interval)</th>
<th>values are Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin aspart pump (N=66)</td>
<td>8.2 ± 1.4</td>
<td>-0.6 ± 1.1</td>
<td>0.1 (0.3, 0.4)</td>
<td></td>
</tr>
<tr>
<td>Insulin aspart + NPH (N=61)</td>
<td>8.0 ± 1.1</td>
<td>-0.5 ± 0.9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are Mean ± SD

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

Insulin aspart 100 units of insulin aspart per mL (U-100) is available as a clear and colorless solution for injection:

- 10 mL multiple-dose vial: NDC 73070-100-11
- 3 mL single-patient-use PenFill® cartridges: NDC 73070-102-15
- 3 mL single-patient-use Insulin Aspart FlexPen®: NDC 73070-103-15

*Insulin Aspart FlexPen® cartridges are designed for use with Novo Nordisk insulin delivery devices with NovoFine® disposable needles. FlexPen® can be used with NovoFine® or NovoTwist® disposable needles.

The Insulin Aspart FlexPen® diats in 1-unit increments.

16.2 Recommended Storage

Dispense in the original sealed carton with the enclosed Instructions for Use.

Unused insulin aspart should be stored in a refrigerator between 2° and 8°C (36° to 46°F). Do not freeze insulin aspart and do not use insulin aspart if it has been frozen. Do not expose insulin aspart to excessive heat or light. Insulin aspart should not be drawn into a syringe and stored for later use. Always remove and discard the needle after each injection from the Insulin Aspart FlexPen® and store without a needle attached. This prevents contamination and/or infection, or leakage of insulin, and will ensure accurate dosing.

The storage conditions are summarized in the following table:

Table 9. Storage conditions for vial, PenFill® cartridges, and Insulin Aspart FlexPen®

<table>
<thead>
<tr>
<th>Insulin aspart presentation</th>
<th>Not-in-use (unopened)</th>
<th>In-use (open)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Room Temperature (below 30°C)</td>
<td>Room Temperature (below 30°C)</td>
<td>Refrigerated (room temperature)</td>
</tr>
<tr>
<td>10 mL multiple-dose vial</td>
<td>Until expiration date</td>
<td>28 days</td>
</tr>
<tr>
<td>3 mL single-patient-use PenFill® cartridges</td>
<td>Until expiration date</td>
<td>28 days (Do not refrigerate)</td>
</tr>
<tr>
<td>3 mL single-patient-use Insulin Aspart FlexPen®</td>
<td>Until expiration date</td>
<td>28 days (Do not refrigerate)</td>
</tr>
</tbody>
</table>

Storage in External Insulin Pump:

Insulin aspart in the pump reservoir should be discarded after at least every 6 days of use or after exposure to temperatures that exceed 37°C (98.6°F). The infusion set and the infusion set insertion site should be changed at least every 3 days.

Storage of Diluted insulin aspart

Insulin aspart diluted with Insulin Diluting Medium for NovoLog® to a concentration equivalent to U-10 to equivalent to U-50 prepared as indicated under Dosage and Administration (2.2) may remain in patient use at temperatures below 30°C (86°F) for 28 days.

Storage of insulin aspart in Intravenous Infusion Fluids

Infusion bags prepared as indicated under Dosage and Administration (2.2) are stable at room temperature for 24 hours. Some insulin will be initially adsorbed to the material of the infusion.

17 PATIENT COUNSELING INFORMATION

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

Never Share an Insulin Aspart FlexPen®, PenFill® Cartridge or PenFill® Cartridge Device Between Patients

Advise patients that they must never share Insulin Aspart FlexPen®, 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 insulin 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 hyperglycemia is the most common adverse reaction with insulin. Inform patients on self-management procedures including glucose monitoring, proper injection technique, and management of hyperglycemia and hypoglycemia, especially at initiation of insulin aspart 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. Inform patients on the management of hyperglycemia (see Warnings and Precautions (5.3)).

Hypoglycemia with Medication Errors

Inform 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)).

Hypoglycemia with Medication Errors

Advise patients on the management of hypoglycemia (see Warnings and Precautions (5.4)).

Administration

Insulin aspart must only be used if the solution is clear and colorless with no particles visible. Instruct patients that when injecting insulin aspart, they must press and hold down the dose button until the dose counter shows 0 and then keep the needle in the skin and count slowly to 6 as the prescribed dose is not completely delivered until 6 seconds later. If the needle is removed earlier, the full dose may not be delivered (a possible under-dose may occur by as much as 20%). Inform the patient to increase underdosing if the dose is not delivered in full. Instruct patients to increase the frequency of checking their blood glucose and that possible additional insulin administration may be necessary.

If does not appear in the dose counter after continuously pressing the dose button, the patient may have used a blocked needle. In this case they would not have received any insulin – even though the dose counter has moved from the original dose that was set. Instruct the patient to change the needle as described in Section 5 of the Instructions for Use and repeat all steps in the IFU starting with Section 1. Prepare your pen with a new needle. Make sure the patient has the full dose needed.

Patients Using Continuous Subcutaneous Insulin Pumps

- Train patients in both intensive insulin therapy with multiple injections and in the function of their pump and pump accessories.

- Instruct patients to replace insulin in the reservoir at least every 6 days; infusion sets and infusion set insertion sites should be changed at least every 3 days. By following this schedule, patients avoid insulin degradation, infusion set occlusion, and loss of the insulin preservative. Insulin aspart is recommended for use in any reservoir and infusion sets that are compatible with insulin and the specific pump. Please see recommended reservoir and infusion sets in the pump manual.

- 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 insulin solution enters becomes erythematous, pruritic, or thickened.

- Instruct patients of the risk of rapid hyperglycemia and ketosis due to pump malfunction, infusion set occlusion, leakage, disconnection or kinking, and degraded insulin. If these problems cannot be promptly corrected, instruct patients to resume therapy with subcutaneous insulin injection and contact their physician (see Warnings and Precautions (5.1) and How Supplied/Storage and Handling (16.2)).

- Instruct patients of 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 (5.1)).

- Advise patients that they must never share Insulin Aspart FlexPen®, 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 insulin 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)).

Always remove and discard the needle after each injection from the Insulin Aspart FlexPen® and store without a needle attached. This prevents contamination and/or infection, or leakage of insulin, and will ensure accurate dosing.
Do not share your Insulin Aspart FlexPen®, 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.

What is insulin aspart?
- Insulin aspart is a man-made insulin that is used to control high blood sugar in adults and children with diabetes mellitus.

Who should not take insulin aspart?
Do not take insulin aspart if you:
- are having an episode of low blood sugar (hypoglycemia).
- have an allergy to insulin aspart or any of the ingredients in insulin aspart.

Before taking insulin aspart, tell your healthcare provider about all your medical conditions including, if you are:
- pregnant, planning to become pregnant, or are breastfeeding.
- taking new prescription or over-the-counter medicines, vitamins, or herbal supplements.

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

How should I take insulin aspart?
- Read the Instructions for Use that come with your insulin aspart.
- Take insulin aspart exactly as your healthcare provider tells you to.
- Insulin aspart starts acting fast. You should eat a meal within 5 to 10 minutes after you take your dose of insulin aspart.
- 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.
- 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 your needles with other people. You may give other people a serious infection or get a serious infection from them.
- Insulin aspart can be injected under the skin (subcutaneously) of your stomach area (abdomen), buttocks, upper legs (thighs) 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 exact same 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 insulin aspart?
While taking insulin aspart do not:
- Drive or operate heavy machinery, until you know how insulin aspart affects you.
- Drink alcohol or use prescription or over-the-counter medicines that contain alcohol.

What are the possible side effects of insulin aspart?
Insulin aspart 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
- sweating
- confusion
- headache
- increased stress

Your insulin dose may need to change because of:
- weight gain or loss
- increased stress

Other common side effects of insulin aspart may include:
- low potassium in your blood (hypokalemia), reactions at the injection site, itching, rash, serious allergic reactions (whole body reactions), skin thickening or pits at the injection site (lipodystrophy), weight gain, and swelling of your hands and feet.

Get emergency medical help if you have:
- trouble breathing, shortness of breath, fast heartbeat, swelling of your face, tongue, or throat, sweating, extreme drowsiness, dizziness, confusion.

These are not all the possible side effects of insulin aspart. 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 insulin aspart.
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 insulin aspart that is written for health professionals. Do not use insulin aspart for a condition for which it was not prescribed. Do not give insulin aspart to other people, even if they have the same symptoms that you have. It may harm them.

What are the ingredients in insulin aspart?
Active Ingredient: insulin aspart
Inactive Ingredients: glycerin, phenol, metacresol, zinc, disodium hydrogen phosphate dihydrate, sodium chloride and water for injection
Manufactured by:
Novo Nordisk A/S, DK-2880 Bagsvaerd, Denmark

For more information, call 1-800-727-6500.

This Patient Information has been approved by the U.S. Food and Drug Administration.
Revised: 11/2019
Instructions for Use
Insulin Aspart Injection
10 mL multiple-dose vial (100 Units/mL, U-100)

Read this Instructions for Use before you start taking insulin aspart 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.

Supplies you will need to give your insulin aspart injection:

- 10 mL insulin aspart vial
- Insulin syringe and needle
- Alcohol swabs

Preparing your insulin aspart dose:

- Wash your hands with soap and water.
- Before you start to prepare your injection, check the insulin aspart label to make sure you are taking the right type of insulin. This is especially important if you use more than 1 type of insulin.
- Insulin aspart should look clear and colorless. Do not use insulin aspart if it is thick, cloudy, or is colored.
- Do not use insulin aspart 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 black tip 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 insulin aspart vial (See Figure D).

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

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

Step 7: Slowly push the plunger up until the black tip reaches the line for your insulin aspart dose (See Figure H).

Step 8: Check the syringe to make sure you have the right dose of insulin aspart.

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

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

Step 11: Insert the needle into your skin. Push down on the plunger to inject your dose (See Figure K). The needle should remain in the skin for at least 6 seconds to make sure you have injected all the insulin.

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

Giving your Injection:

- Inject your insulin aspart exactly as your healthcare provider has shown you. Your healthcare provider should tell you if you need to pinch the skin before injecting.
- Insulin aspart can be injected under the skin (subcutaneously) of your stomach area, buttocks, upper legs or upper arms, infused in an insulin pump (continuous subcutaneous infusion 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.
- If you inject insulin aspart, 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.
- If you use insulin aspart in an insulin pump, you should change your insertion site every 3 days. Insulin aspart should be given into an area of your body recommended in the instructions that come with your insulin pump. Change (rotate) your insertion sites within the area you choose for each insertion to reduce your risk of getting lipodystrophy (pits in skin or thickened skin) and localized cutaneous amyloidosis (skin with lumps) at the insertion sites. Do not inject into the exact same spot for each insertion. 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. 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 insulin aspart in an insulin pump, see your insulin pump manual for instructions or talk to your healthcare provider.

After your injection:

- Do not recap the needle. Recapping the needle can lead to a needle stick injury.
- Put the empty insulin vials, used needles and syringes in a FDA-cleared sharps disposal container right away after use. Do not throw away (dispose of) loose needles and syringes and needles 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 heavy-duty plastic,
  - can be closed with a tight-fitting, puncture-resistant lid, without sharp 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. 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.

How should I store insulin aspart?

- Do not freeze insulin aspart. Do not use insulin aspart if it has been frozen.
- Keep insulin aspart away from heat or light.

All unopened vials:

- Store unopened insulin aspart vials in the refrigerator at 36°F to 46°F (2°C to 8°C).
- Unopened vials may be used until the expiration date printed on the label, if they have been stored in the refrigerator.
- Unopened vials should be thrown away after 28 days, if they are stored at room temperature.
• **After vials have been opened:**
  - Opened insulin aspart 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 insulin aspart vials after 28 days, even if they still have insulin left in them.

**General information about the safe and effective use of insulin aspart**
- Always use a new syringe and needle for each injection.
- Do not share syringes or needles.
- Keep insulin aspart vials, syringes, and needles out of the reach of children.
Instructions For Use

Insulin Aspart FlexPen®

Injection

Introduction

Please read the following instructions carefully before using your Insulin Aspart FlexPen®.

Do not share your Insulin Aspart FlexPen® 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.

Insulin Aspart FlexPen® is a disposable, single-patient, use-dial-a-dose insulin pen. You can select doses from 1 to 60 units in increments of 1 unit. Insulin Aspart FlexPen® is designed to be used with NovoFine®, NovoFine® Plus or NovoTwist® needles.

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

Getting ready

Make sure you have the following items:

- Insulin Aspart FlexPen®
- New NovoFine®, NovoFine® Plus or NovoTwist® needle
- Alcohol swabs

Insulin Aspart FlexPen®

Pen cap

Rubber stopper

Cartridge

Cartridge scale

Pointer

Dose button

Push-button
dose selector

NovoFine®
Big outer needle cap

Inner needle cap

Needle

Protective tab

NovoFine® Plus
Big outer needle cap

Inner needle cap

Needle

Protective tab

NovoTwist®
Big outer needle cap

Inner needle cap

Needle

Protective tab

Preparing your Insulin Aspart FlexPen®

Wash your hands with soap and water. Before you start to prepare your injection, check the label to make sure that you are taking the right type of insulin. This is especially important if you take more than 1 type of insulin. Insulin aspart should look clear and the right type of insulin. This is especially important if you take a different type of insulin. This is especially important if you take more than 1 type of insulin. Insulin aspart should look clear and the right type of insulin. This is especially important if you take a different type of insulin.

A. Pull off the pen cap (see diagram A).

Wipe the rubber stopper with an alcohol swab.

B. Attaching the needle

Remove the protective tab from a disposable needle. Screw the needle tightly onto your FlexPen®. It is important that the needle is put on straight (see diagram B). Never place a disposable needle on your Insulin Aspart FlexPen® until you are ready to take your injection.

C. Pull off the big outer needle cap (see diagram C).

NovoFine®

NovoFine® Plus

NovoTwist®

D. Pull off the inner needle cap and throw it away (dispose of it) (see diagram D).

E. Turn the dose selector to select 2 units (see diagram E).

F. Hold your Insulin Aspart FlexPen® with the needle pointing up. Tap the cartridge gently with your finger a few times to make any air bubbles collect at the top of the cartridge (see diagram F).

G. Keep the needle pointing upwards, press the push-button all the way in (see diagram G). The dose selector returns to 0.

A drop of insulin should appear at the needle tip. If not, change the needle and repeat the procedure no more than 6 times.

If you do not see a drop of insulin after 6 times, do not use the Insulin Aspart FlexPen® and contact Novo Nordisk at 1-800-727-4500.

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

Selecting your dose

Check and make sure that the dose selector is set at 0.

H. Turn the dose selector to the number of units you need to inject.

The pointer should line up with your dose. The dose can be corrected either up or down by turning the dose selector in either direction until the correct dose lines up with the pointer (see diagram H). When turning the dose selector, be careful not to press the push-button as insulin will come out.

You cannot select a dose larger than the number of units left in the cartridge.

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.

I. Insert the needle into your skin.

Inject the dose by pressing the push-button all the way in until the 0 lines up with the pointer (see diagram I). Be careful only to push the button when injecting.

Turning the dose selector will not inject insulin.

J. Keep the needle in the skin for at least 6 seconds, and keep the push-button pressed all the way in until the needle has been pulled out from the skin (see diagram J). This will make sure that the full dose has been given.

You may see a drop of insulin at the needle tip. 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 an alcohol swab. Do not rub the area.

After the injection

Do not recap the needle. Recapping can lead to a needle stick injury. Remove the needle from the Insulin Aspart FlexPen®after each injection and dispose of it. This helps to prevent infection, leakage of insulin, and will help to make sure you inject the right dose of insulin.

If you do not have a sharps container, carefully slip the needle into the outer needle cap. Safely remove the needle and throw it away as soon as you can.

- Put your used needles in a FDA-cleared sharps disposal container right away after use. Do not throw away (dispose of) loose needles 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. 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.
- When there is not enough medicine left in your Insulin Aspart FlexPen® for your prescribed dose, the Insulin Aspart FlexPen®may be thrown away in your household trash after you have removed the needle.

The Insulin Aspart FlexPen® prevents the cartridge from being completely emptied. It is designed to deliver 300 units.

K. Put the pen cap on the Insulin Aspart FlexPen® and store the Insulin Aspart FlexPen® without the needle attached (see diagram K). Storing without the needle attached helps prevent leaking, blocking of the needle, and air from entering the Pen.

△ Do not use the cartridge scale printed on the cartridge to measure your dose of insulin.

Giving the injection

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. Wipe the skin with an alcohol swab and let the area dry.

Insulin aspart can be injected under the skin (subcutaneously) of your stomach area, buttocks, upper legs (thighs), or upper arms. 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.

- Insert the needle into your skin.
- Inject the dose by pressing the push-button all the way in until the 0 lines up with the pointer (see diagram I). Be careful only to push the button when injecting.
- Turning the dose selector will not inject insulin.
- Keep the needle in the skin for at least 6 seconds, and keep the push-button pressed all the way in until the needle has been pulled out from the skin (see diagram J). This will make sure that the full dose has been given.
- You may see a drop of insulin at the needle tip. 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 an alcohol swab. Do not rub the area.

After the injection

Do not recap the needle. Recapping can lead to a needle stick injury. Remove the needle from the Insulin Aspart FlexPen®after each injection and dispose of it. This helps to prevent infection, leakage of insulin, and will help to make sure you inject the right dose of insulin.

If you do not have a sharps container, carefully slip the needle into the outer needle cap. Safely remove the needle and throw it away as soon as you can.

- Put your used needles in a FDA-cleared sharps disposal container right away after use. Do not throw away (dispose of) loose needles 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. 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.
- When there is not enough medicine left in your Insulin Aspart FlexPen® for your prescribed dose, the Insulin Aspart FlexPen®may be thrown away in your household trash after you have removed the needle.

The Insulin Aspart FlexPen® prevents the cartridge from being completely emptied. It is designed to deliver 300 units.

K. Put the pen cap on the Insulin Aspart FlexPen® and store the Insulin Aspart FlexPen® without the needle attached (see diagram K). Storing without the needle attached helps prevent leaking, blocking of the needle, and air from entering the Pen.

△ Do not use the cartridge scale printed on the cartridge to measure your dose of insulin.

Giving the injection

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. Wipe the skin with an alcohol swab and let the area dry.

Insulin aspart can be injected under the skin (subcutaneously) of your stomach area, buttocks, upper legs (thighs), or upper arms. 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.

- Insert the needle into your skin.
- Inject the dose by pressing the push-button all the way in until the 0 lines up with the pointer (see diagram I). Be careful only to push the button when injecting.
- Turning the dose selector will not inject insulin.
- Keep the needle in the skin for at least 6 seconds, and keep the push-button pressed all the way in until the needle has been pulled out from the skin (see diagram J). This will make sure that the full dose has been given.
- You may see a drop of insulin at the needle tip. 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 an alcohol swab. Do not rub the area.
How should I store Insulin Aspart FlexPen®?

- **Do not** freeze insulin aspart. **Do not** use insulin aspart if it has been frozen.
- Keep insulin aspart away from heat or light.
- Store the Insulin Aspart FlexPen® without the needle attached.

**Until first use:**
- Store unused Insulin Aspart FlexPen® in the refrigerator at 36°F to 46°F (2°C to 8°C).
- Unused FlexPen® may be used until the expiration date printed on the label, if kept in the refrigerator.
- Unused Insulin Aspart FlexPen® stored at room temperature should be thrown away after 28 days.

**In-use:**
- Store the FlexPen® you are currently using out of the refrigerator at room temperature below 86°F (30°C) for up to 28 days.
- The Insulin Aspart FlexPen® you are using should be thrown away after 28 days, even if it still has insulin left in it.

**Maintenance**

For the safe and proper use of your FlexPen®, be sure to handle it with care. Avoid dropping your FlexPen® as it may damage it. If you are concerned that your FlexPen® is damaged, use a new one. You can clean the outside of your FlexPen® by wiping it with a damp cloth. Do not soak or wash your FlexPen® as it may damage it. Do not refill your FlexPen®.

- Remove the needle from the Insulin Aspart FlexPen® after each injection. This helps to ensure sterility, prevent leakage of insulin, and will help to make sure you inject the right dose of insulin for future injections.
- Be careful when handling used needles to avoid needle sticks and transfer of infectious diseases.
- Keep your Insulin Aspart FlexPen® and needles out of the reach of children.
- Use Insulin Aspart FlexPen® as directed to treat your diabetes.
- **Do not** share your Insulin Aspart FlexPen® or needles with other people. You may give other people a serious infection, or get a serious infection from them.
- Always use a new needle for each injection.
- Novo Nordisk is not responsible for harm due to using this insulin pen with products not recommended by Novo Nordisk.
- As a precautionary measure, always carry a spare insulin delivery device in case your Insulin Aspart FlexPen® is lost or damaged.
- Remember to keep the disposable Insulin Aspart FlexPen® with you. Do not leave it in a car or other location where it can get too hot or too cold.
Supplies you will need to give your insulin aspart injection

- 1 new NovoFine®
- Insulin Aspart PenFill® cartridge compatible insulin delivery device
- 1 new NovoFine®, NovoFine® Plus, or NovoTwist® needle
- Alcohol swabs
- Adhesive bandage
- Cauter gauze
- A sharp container for throwing away used PenFill® cartridges and needles. See “After your injection” at the end of these instructions.

How to use the insulin Aspart PenFill® cartridge

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).
2. 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.
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.
4. Push the needle straight onto the device. Turn the needle clockwise until it is on tight (See Figure B).
5. Insert the 3 mL cartridge with the threaded end first into your Novo Nordisk 3 mL PenFill® cartridge compatible insulin delivery device (See Figure C).
6. Carefully look at the cartridge and the insulin inside it. Check that the insulin aspart cartridge:
   - is not damaged, for example cracked or leaking
   - is not loose on the threaded end
7. Insulin aspart should look clear and colorless. Do not use insulin aspart if it is cloudy or colored or if the threaded end is loose (See Figure B).
8. Wash your hands with soap and water.
9. Before you start to prepare your injection, check the insulin Aspart 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.
10. 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.
11. If the insulin Aspart PenFill® cartridge has already been used, start with Step 2.
12. Do not attach your PenFill to your device until you are ready to give your injection. Do not re-use or share your needles with other people. You may give others a serious infection, or get a serious infection from them.
13. Be careful not to bend or damage the needle before you use it.
14. Insert the needle through the skin where 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.
15. Clean your injection site with an alcohol swab. Let your skin dry. Do not touch this area again before injecting.
16. 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).
17. 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.
18. Do the airshot as described in the instruction manual that comes with your device.
19. 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 1: Check to make sure that the dose counter is set to 0.
Step 2: 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.
Step 3: Refer to your insulin delivery device manual if necessary.

Inject your dose

Step 1: 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.
Step 2: Insulin aspart can be injected under the skin (subcutaneously) of your stomach area (abdomen), buttocks, upper legs (thighs), or upper arms (See Figure I).
Step 3: 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 4: Clean your injection site with an alcohol swab. Let your skin dry. Do not touch this area again before injecting.
Step 5: 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 insulin aspart 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 tightly with a cotton gauge 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.

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.
• The Insulin Aspart 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 insulin aspart.
• Keep Insulin Aspart PenFill® cartridges and needles out of the reach of children.
• Do not share Insulin Aspart 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.