NOVOLOG- insulin aspart injection, solution
INSULIN DILUTING MEDIUM FOR NOVOLOG- water injection injection, solution
Novo Nordisk

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

- NOVOLOG 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 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 NOVOLOG 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 NOVOLOG to concentrations from 0.05 unit/mL to 1 unit/mL insulin aspart in infusion systems using polypropylene infusion bags.
  - NOVOLOG is stable in infusion fluids such as 0.9% sodium chloride.
- Individualize and adjust the dosage of NOVOLOG 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 NOVOLOG FlexPen® (3)
- 3 mL single-patient-use NOVOLOG FlexTouch® (3)

CONTRAINDICATIONS

- During episodes of hypoglycemia (4).

- Hypersensitivity to NOVOLOG or one of its excipients.

WARNINGS AND PRECAUTIONS

- *Never share* a NOVOLOG FlexPen or a NOVOLOG FlexTouch, 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 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 NOVOLOG, 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).
- *Fluidretention 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 NOVOLOG by subcutaneous injection if pump malfunction occurs (5.8).

ADVERSE REACTIONS

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

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 may increase the risk of hypoglycemia:* antidiabetic agents, ACE inhibitors, angiotensin II receptor blocking agents, disopyramide, fibrates, 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, danazol, diuretics, estrogens, glucagon, isoniazid, 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 (8.4).

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

Revised: 11/2019

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

NOVOLOG is a rapid acting human insulin analog indicated to improve glycemic control in adults 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 NOVOLOG visually before use. It should appear clear and colorless. Do not use NOVOLOG if particulate matter or coloration is seen.
- Use NOVOLOG FlexPen and NOVOLOG FlexTouch 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 NOVOLOG with other insulins when administering using a continuous subcutaneous infusion pump.

2.2 Route of Administration

Subcutaneous Injection

- Inject NOVOLOG 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 NOVOLOG FlexPen and FlexTouch dial in 1-unit increments.
- NOVOLOG administered by subcutaneous injection should generally be used in regimens with an intermediate- or long-acting insulin.
- NOVOLOG may be diluted with Insulin Diluting Medium for NOVOLOG for subcutaneous injection. Diluting one part NOVOLOG to nine parts diluent will yield a concentration one-tenth that of NOVOLOG (equivalent to U-10). Diluting one part NOVOLOG to one part diluent will yield a concentration one-half that of NOVOLOG (equivalent to U-50).

Continuous Subcutaneous Infusion (Insulin Pump)

- Use NOVOLOG in pump systems specifically indicated for insulin infusion.
- Train patients using continuous subcutaneous insulin fusion pump therapy to administer insulin by injection and have alternate insulin therapy available in case of pump failure.
- Administer NOVOLOG 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 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)]*.

- Follow healthcare provider recommendations when setting basal and meal time infusion rate.
- Change the NOVOLOG in the reservoir at least every 6 days. Follow the NOVOLOG-specific information for in-use time because NOVOLOG-specific information may differ from general pump manual instructions.
- Change the infusion set and the infusion set insertion site at least every 3 days.
- Do NOT dilute or mix NOVOLOG when administering by continuous subcutaneous infusion.
- Do NOT expose NOVOLOG in the pump reservoir to temperatures greater than 98.6°F (37°C).

Intravenous Administration

- Dilute NOVOLOG to concentrations from 0.05 unit/mL to 1 unit/mL insulin aspart in infusion systems using polypropylene infusion bags. NOVOLOG is stable in infusion fluids such as 0.9% sodium chloride.
- Administer NOVOLOG 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 NOVOLOG based on route of administration, the individual's metabolic needs, blood glucose monitoring results and glycemic control goal.
- 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 NOVOLOG *[see Warnings and Precautions (5.2)]*.

2.4 Dosage Adjustment Due to Drug Interactions

- Dosage adjustment may be needed when NOVOLOG is co-administered with certain drugs *[see Drug Interactions (7)]*.

2.5 Instructions for Mixing with Other Insulins

NOVOLOG subcutaneous injection route	NOVOLOG may be mixed with NPH insulin preparations **ONLY**. **• If NOVOLOG is mixed with NPH insulin, draw NOVOLOG into the syringe first and inject immediately after mixing.**
NOVOLOG continuous subcutaneous infusion route (Insulin Pump)	Do NOT mix **NOVOLOG with any other insulin.**

3 DOSAGE FORMS AND STRENGTHS

NOVOLOG 100 units per mL (U-100) is available as a clear and colorless solution for injection in:

- 10 mL multiple-dose vial
- 3 mL single-patient-use PenFill cartridges for the 3 mL PenFill cartridge delivery device with NovoFine® disposable needles

- 3 mL single-patient-use NOVOLOG FlexPen
- 3 mL single-patient-use NOVOLOG FlexTouch

4 CONTRAINDICATIONS

NOVOLOG is contraindicated:

- During episodes of hypoglycemia *[see Warnings and Precautions (5.3)]*
- In patients with hypersensitivity to NOVOLOG or one of its excipients, *[see Warnings and Precautions (5.5)]*

5 WARNINGS AND PRECAUTIONS

5.1 Never Share a NOVOLOG FlexPen, NOVOLOG FlexTouch, PenFill Cartridge, or PenFill Cartridge Device between Patients

NOVOLOG FlexPen, NOVOLOG FlexTouch, PenFill cartridge, and PenFill cartridge devices should never be shared between patients, even if the needle is changed. Patients using NOVOLOG 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 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 of concomitant anti-diabetic products may be needed.

5.3 Hypoglycemia

Hypoglycemia is the most common adverse effect of all insulin therapies, including NOVOLOG. 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 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. As with all insulin preparations, the glucose lowering effect time course of NOVOLOG may vary in different individuals or at different times in the same individual and depends on many conditions, including the area of

injection as well as the injection site blood supply and temperature *[see Clinical Pharmacology (12.2)]*. 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; increased frequency of blood glucose monitoring is recommended. 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 NOVOLOG and other insulin products have been reported. To avoid medication errors between NOVOLOG and other insulins, instruct patients to always check the insulin label before each injection.

5.5 Hypersensitivity and Allergic Reactions

Severe, life-threatening, generalized allergy, including anaphylaxis, can occur with insulin products, including NOVOLOG. If hypersensitivity reactions occur, discontinue NOVOLOG; treat per standard of care and monitor until symptoms and signs resolve *[see Adverse Reactions (6)]*. NOVOLOG 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 NOVOLOG, 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 NOVOLOG, 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

Malfunction of the insulin pump or insulin 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 NOVOLOG 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 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 NOVOLOG 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 NOVOLOG in one clinical trial with a mean exposure duration to NOVOLOG 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 25.6 kg/m^2. The mean duration of diabetes was 15.7 years and the mean HbA_{1c} at baseline was 7.9%.

The data in Table 2 reflect the exposure of 91 patients with type 2 diabetes to NOVOLOG in one clinical trial with a mean exposure duration to NOVOLOG 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 29.7 kg/m^2. The mean duration of diabetes was 12.7 years and the mean HbA_{1c} 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 NOVOLOG-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 Table 1 and Table 2, respectively.

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

	NOVOLOG + NPH (%) (n= 596)	**Regular Human Insulin + NPH (%) (n= 286)**
Headache	12	10
Injury accidental	11	10
Nausea	7	5
Diarrhea	5	3

Table 2: Adverse reactions occurring in ≥ 5% of Type 2 Diabetes Mellitus Adult Patients treated with NOVOLOG and at the same rate or greater on NOVOLOG than on comparator

	NOVOLOG + NPH (%) (n= 91)	**Human Regular Insulin + NPH (%) (n= 91)**
Hyporeflexia	11	7
Onychomycosis	10	5
Sensory disturbance	9	7
Urinary tract infection	8	7
Chest pain	5	3
Headache	5	3

Skin disorder	5	2
Abdominal pain	5	1
Sinusitis	5	1

Severe hypoglycemia

Hypoglycemia is the most commonly observed adverse reaction in patients using insulin, including NOVOLOG *[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 NOVOLOG with the incidence of hypoglycemia for other products may be misleading and also, may not be representative of hypoglycemia rates that will occur in clinical practice.

Severehypoglycemia 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 NOVOLOG with type 1 diabetes mellitus was 17% at 24 weeks and 6% at 24 weeks, respectively *[see Clinical Studies (14)]*.

The incidence of severe hypoglycemia in adult patients receiving subcutaneous NOVOLOG 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 NOVOLOG 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 NOVOLOG via continuous subcutaneous insulin infusion by external pump at 16 weeks.

Allergic Reactions

Some patients taking insulin therapy, including NOVOLOG 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 initiation and glucose control intensification

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

Lipodystrophy

Administration of insulin, including NOVOLOG, subcutaneously and via subcutaneous insulin infusion by external pump, has resulted in lipoatrophy (depression in the skin) or lipohypertrophy (enlargement or thickening of tissue) in some patients *[see Dosage and Administration (2.2)]*.

Peripheral Edema

Insulin products, including NOVOLOG, 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 NOVOLOG 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 NOVOLOG 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, 99.8% of patients who received NOVOLOG 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 NOVOLOG were positive for anti-drug antibodies (ADA) at least once during the study, including 64.6% that were positive at baseline.

In a phase 3 type 1 diabetes clinical trial of NOVOLOG, 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 or necessitate increases in insulin dose.

6.3 Post Marketing Experience

The following adverse reactions have been identified during post-approval use of NOVOLOG. 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 accidentally substituted for NOVOLOG *[see Warnings and Precautions (5.4)]*.

Localized cutaneous amyloidosis at the injection site has occurred with insulin aspart. 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

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, propoxyphene, salicylates, somatostatin analog (e.g., octreotide), and sulfonamide antibiotics.
Intervention:	Dose adjustment and increased frequency of glucose monitoring may be required when NOVOLOG is co-administered with these drugs.
Drugs That May Decrease the Blood Glucose Lowering Effect of NOVOLOG	
Drugs:	Atypical antipsychotics (e.g., olanzapine and clozapine), corticosteroids, danazol, diuretics, estrogens, glucagon, isoniazid, niacin, oral contraceptives, phenothiazines, progestogens (e.g., in oral contraceptives), protease inhibitors, somatropin, sympathomimetic agents (e.g., albuterol, epinephrine, terbutaline), and thyroid hormones.
Intervention:	Dose adjustment and increased frequency of glucose monitoring may be required when NOVOLOG is co-administered with these drugs.
Drugs That May Increase or Decrease the Blood Glucose Lowering Effect of NOVOLOG	
Drugs:	Alcohol, beta-blockers, clonidine, and lithium salts. Pentamidine may cause hypoglycemia, which may sometimes be followed by

	hyperglycemia. Pentamidine may cause hypoglycemia, which may sometimes be followed by hyperglycemia.
Intervention:	Dose adjustment and increased frequency of glucose monitoring may be required when NOVOLOG 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 NOVOLOG 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 reported an association with insulin aspart and major birth defects or adverse maternal or fetal outcomes *[see Data]*. There are risks to the mother and fetus associated with poorly controlled diabetes in pregnancy *[see Clinical Considerations]*.

In animal reproduction studies, administration of subcutaneous insulin aspart to pregnant rats and rabbits during the period of organogenesis did not cause adverse developmental effects at exposures 8-times and equal to the human subcutaneous dose of 1 unit/kg/day, respectively. Pre- and post-implantation losses and visceral/skeletal abnormalities were seen at higher exposures, which are considered secondary to maternal hypoglycemia. These effects were similar to those observed in rats administered regular human insulin *[see Data]*.

The estimated background risk of major birth defects is 6-10% in women with pre-gestational diabetes with a HbA_{1c} >7% and has been reported to be as high as 20-25% in women with a HbA_{1c} >10%. The estimated background risk of miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Clinical Considerations

Disease-Associated Maternal and/or Embryo-Fetal Risk

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

Data

Human Data

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

majority of the trials.

Animal Data

Fertility, embryo-fetal and pre- and postnatal development studies have been performed with insulin aspart and regular human insulin in rats and rabbits. In a combined fertility and embryo-fetal development study in rats, insulin aspart was administered before mating, during mating, and throughout pregnancy. Further, in a pre- and postnatal development study insulin aspart was given throughout pregnancy and

during lactation to rats. In an embryo-fetal development study insulin aspart was given to female rabbits during organogenesis. The effects of insulin aspart did not differ from those observed with subcutaneous regular human insulin. Insulin aspart, like human insulin, caused pre- and post-implantation losses and visceral/skeletal abnormalities in rats at a dose of 200 units/kg/day (approximately 32 times the human subcutaneous dose of 1 unit/kg/day, based on human exposure equivalents) and in rabbits at a dose of 10 units/kg/day (approximately three times the human subcutaneous dose of 1 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 rats and equal to the human subcutaneous dose of 1 unit/kg/day for rabbits, based on human exposure equivalents. The effects are considered secondary to maternal hypoglycemia.

8.2 Lactation

Risk Summary

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

8.4 Pediatric Use

NOVOLOG 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)]*. NOVOLOG has not been studied in pediatric patients younger than 2 years of age. NOVOLOG has not been studied in pediatric patients with type 2 diabetes.

8.5 Geriatric Use

Of the total number of patients (n=1,375) treated with NOVOLOG 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 (18/1285) and the other half had type 2 diabetes (18/90). The HbA_{1c} response to NOVOLOG, 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 NOVOLOG dose adjustment and more frequent blood glucose monitoring *[see Warnings and Precautions (5.3) and Clinical Pharmacology (12.3)]*.

8.7 Hepatic Impairment

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

10 OVERDOSAGE

Excess insulin administration may cause hypoglycemia and hypokalemia *[see Warnings and Precautions (5.3, 5.6)]*. 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 carbohydrate intake and observation may be necessary because hypoglycemia may recur after apparent clinical recovery. Hypokalemia must be corrected

appropriately.

11 DESCRIPTION

NOVOLOG (insulin aspart injection) is a rapid-acting human insulin analog used to lower blood glucose. NOVOLOG 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 has the empirical formula $C_{256}H_{381}N_{65}0_{79}S_6$ and a molecular weight of 5825.8.

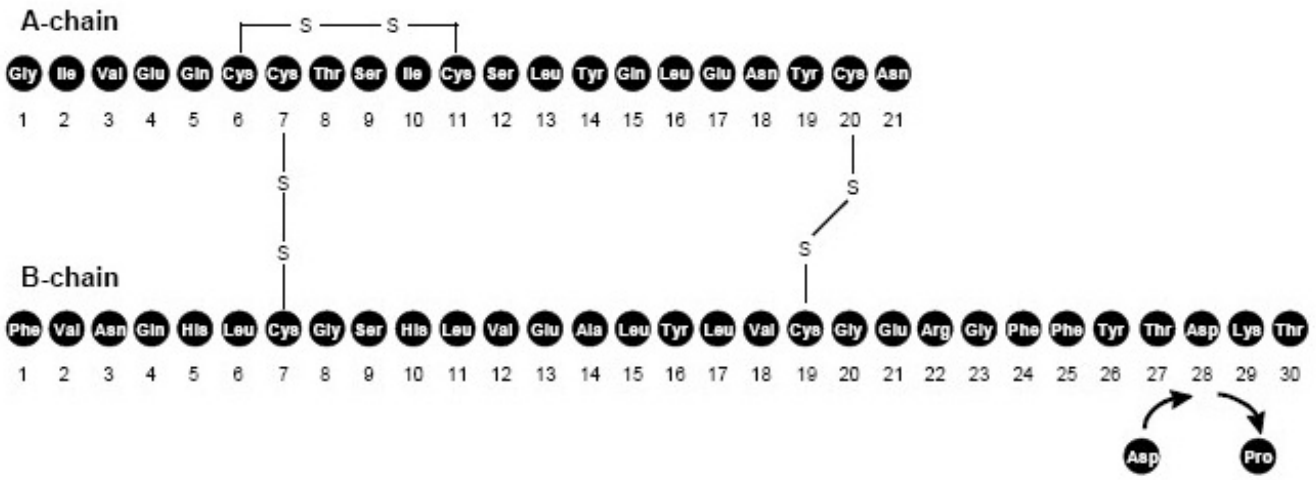

Figure 1. Structural formula of insulin aspart.

NOVOLOG is a sterile, aqueous, clear, and colorless solution, that contains insulin aspart 100 units/mL, glycerin 16 mg/mL, phenol 1.50 mg/mL, metacresol 1.72 mg/mL, zinc 19.6 mcg/mL, disodium hydrogen phosphate dihydrate 1.25 mg/mL, sodium chloride 0.58 mg/mL and water for injection. NOVOLOG has a pH of 7.2-7.6. Hydrochloric acid 10% and/or sodium hydroxide 10% may be added to adjust pH.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The primary activity of insulin, including NOVOLOGis the regulation of glucose metabolism. Insulin and its analogs lower blood glucose by stimulating peripheral glucose uptake, especially by skeletal muscle and fat, and by inhibiting hepatic glucose production. Insulin inhibits lipolysis and proteolysis, and enhances protein synthesis.

12.2 Pharmacodynamics

Subcutaneous administration

The pharmacodynamic profile of NOVOLOG given subcutaneously in 22 patients with type 1 diabetes is shown in Figure 2. The maximum glucose-lowering effect of NOVOLOG occurred between 1 and 3 hours after subcutaneous injection (0.15 units/kg). The duration of action for NOVOLOG is 3 to 5 hours. The time course of action of insulin and insulin analogs such as NOVOLOG may vary considerably in different individuals orwithin the same individual. The parameters of NOVOLOG activity (time of onset, peak time and duration) as designated in Figure 2 should be considered only as general guidelines. The rate of insulin absorption and onset of activity is affected by the site of injection, exercise, and other variables *[see Warnings and Precautions (5.3)]*.

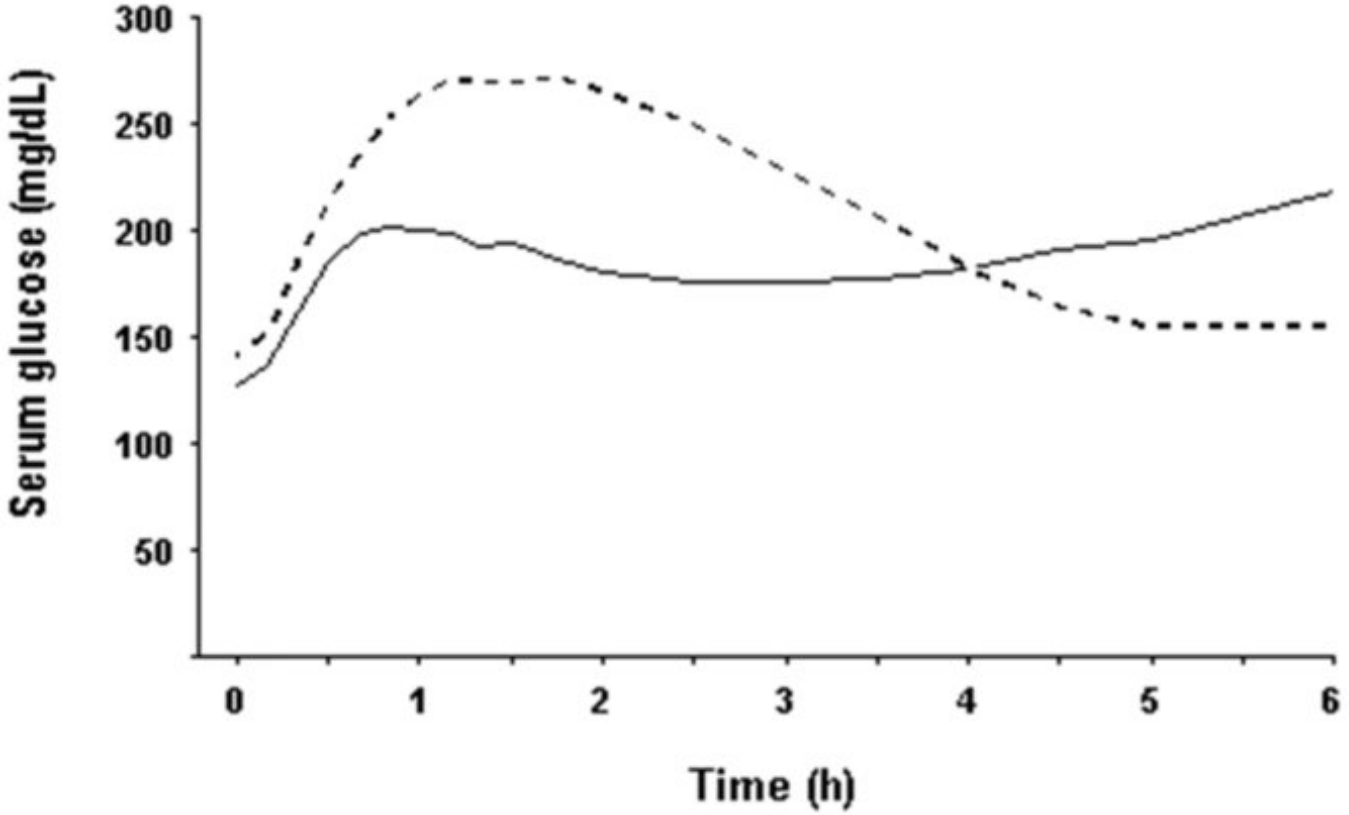

Figure 2. Serial mean serum glucose collected up to 6 hours following a single 0.15 units/kg pre-meal dose of NOVOLOG (solid curve) or regular human insulin (hatched curve) injected immediately before a meal in 22 patients with type 1 diabetes.

Intravenous administration

A double-blind, randomized, two-way crossover study in 16 patients with type 1 diabetes demonstrated that intravenous infusion of NOVOLOG resulted in a blood glucose profile that was similar to that after intravenous infusion with regular human insulin. NOVOLOG 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 sweating), defined as the time of autonomic reaction (R) (see Figure 3).

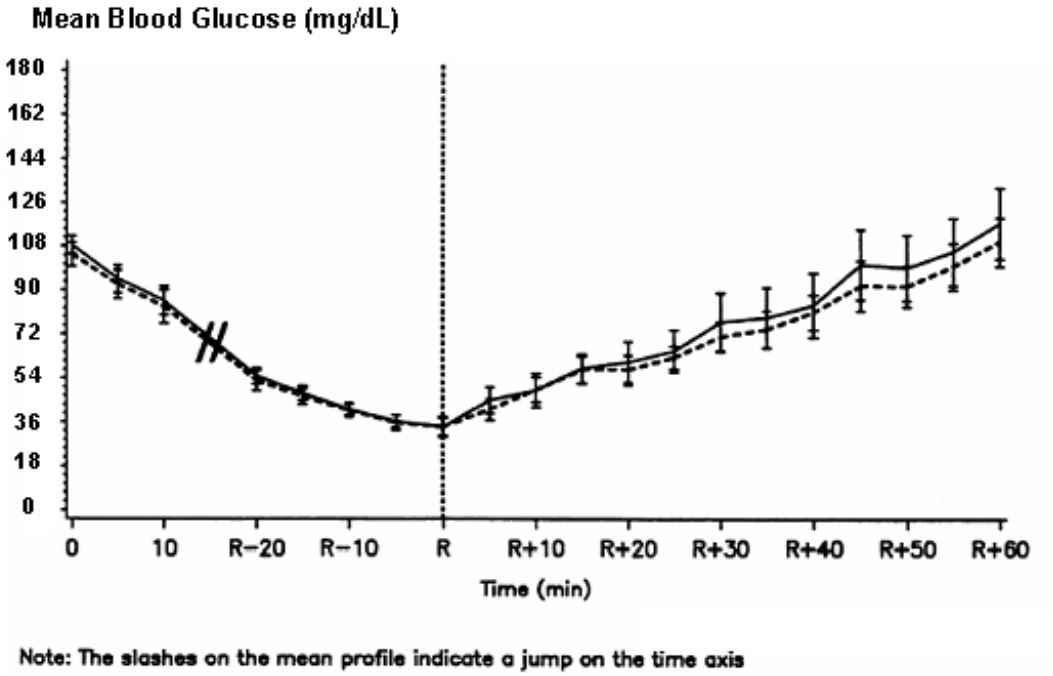

Figure 3. Mean blood glucose profiles following intravenous infusion of NOVOLOG (hatched curve) and regular human insulin (solid curve) in 16 patients with type 1 diabetes. R represents the time of autonomic reaction.

12.3 Pharmacokinetics

Subcutaneous administration

Absorption and Bioavailability

In studies in healthy volunteers (total n=107) and patients with type 1 diabetes (total n=40), the median time to maximum concentration of NOVOLOG in these trials was 40 to 50 minutes versus 80 to 120 minutes, for regular human insulin respectively.

The relative bioavailability of NOVOLOG (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, NOVOLOG and regular human insulin, both administered subcutaneously at a dose of 0.15 units/kg body weight, reached mean maximum concentrations of 82 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.

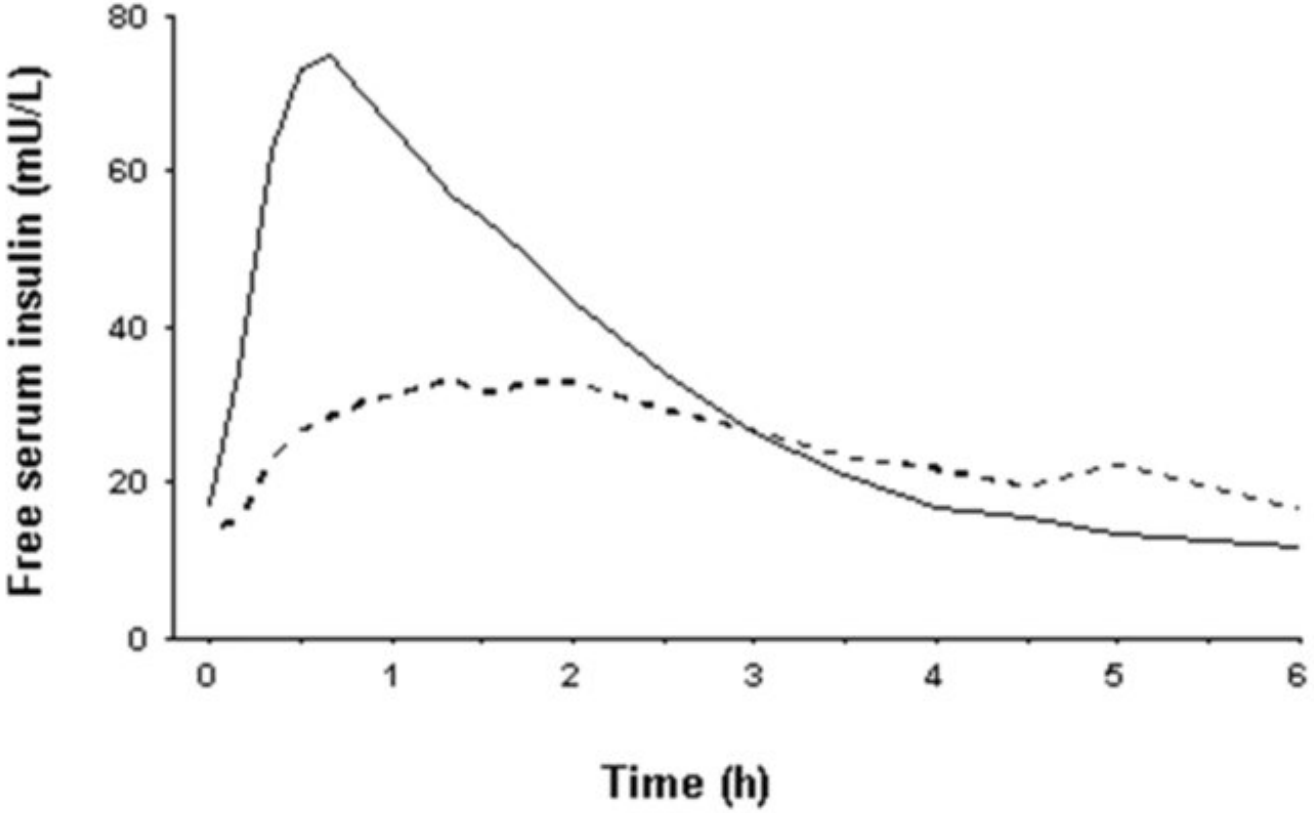

Figure 4. Serial mean serum free insulin concentration collected up to 6 hours following a single 0.15 units/kg pre-meal dose of NOVOLOG (solid curve) or regular human insulin (hatched curve) injected immediately before a meal in 22 patients with type 1 diabetes.

Metabolism and Elimination

In a randomized, double-blind, crossover study 17 healthy Caucasian male subjects between 18 and 40 years of age received an intravenous infusion of either NOVOLOG or regular human insulin at 1.5 mU/kg/min for 120 minutes. The mean insulin clearance was similar for the two groups with mean values of 1.2 L/h/kg for the NOVOLOG group and 1.2 L/h/kg for the regular human insulin group.

After subcutaneous administration in normal malevolunteers (n=24), NOVOLOG was eliminated with an average apparent half-life of 81 minutes.

Specific Populations

Pediatrics - Thepharmacokinetic and pharmacodynamic properties of NOVOLOG and regular humaninsulin were evaluated in asingle dose study in 18 children (6-12 years, n=9) and adolescents (13-17 years [Tanner grade ≥ 2], n=9) with type 1 diabetes. The relative differences in pharmacokinetics and pharmacodynamics in children and adolescents with type 1 diabetes between NOVOLOG and regular human insulin were similar to those in healthy adult subjects and adults with type 1 diabetes.

Geriatrics: The pharmacokinetic and pharmacodynamic properties of NOVOLOG and regular human insulin were investigated in a single dose study in 18 subjects with type 2 diabetes who were ≥ 65 years of age. The relative differences in pharmacokinetics and pharmacodynamics in geriatric patients with type 2 diabetes between NOVOLOG and regular human insulin were similar to those in younger adults.

Gender: Inhealthy volunteers given a single subcutaneous dose of NOVOLOG 0.06 units/kg, no difference in insulin aspart levels was seen between men and women based on comparison of $AUC_{(0-10h)}$ or C_{max}.

Obesity: A single subcutaneous dose of 0.1 units/kg NOVOLOG was administered in a study of 23 patients with type 1 diabetes and a wide range of body mass index (BMI, 22-39 kg/m^2). The

pharmacokinetic parameters, AUC and C_{max}, of NOVOLOG were generally unaffected by BMI in the different groups – BMI 19-23 kg/m^2 (N=4); BMI 23-27 kg/m^2 (N=7); BMI 27-32 kg/m^2 (N=6) and BMI >32 kg/m^2 (N=6). Clearance of NOVOLOG was reduced by 28% in patients with BMI >32 kg/m^2 compared to patients with BMI <23 kg/m^2.

Renal Impairment: A single subcutaneous dose of 0.08 units/kg NOVOLOG was administered in a study to subjects with either normal renal function (N=6) creatinine clearance (CLcr) (> 80 ml/min) or mild (N=7; CLcr = 50-80 ml/min), moderate (N=3; CLcr = 30-50 ml/min) or severe (but not requiring hemodialysis) (N=2; CLcr = <30 ml/min) renal impairment. In this study, there was no apparent effect of creatinine clearance values on AUC and C_{max} of NOVOLOG.

Hepatic Impairment: A single subcutaneous dose of 0.06 units/kg NOVOLOG was administered in an open-label, single-dose study of 24 subjects (N=6/group) with different degree of hepatic impairment (mild, moderate and severe) having Child-Pugh Scores ranging from 0 (healthy volunteers) to 12 (severe hepatic impairment). In this study, there was no correlation between the degree of hepatic impairment and any NOVOLOG pharmacokinetic parameter.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Standard 2-year carcinogenicity studies in animals have not been performed to evaluate the carcinogenic potential of NOVOLOG.In 52-week studies, Sprague-Dawley rats were dosed subcutaneously with NOVOLOG at 10, 50, and 200 units/kg/day (approximately 2, 8, and 32 times the human subcutaneous dose of 1.0 units/kg/day, based on units/body surface area, respectively). At a dose of 200 units/kg/day, NOVOLOG increased the incidence of mammary gland tumors in females when compared to untreated controls. The relevance of these findings to humans is unknown.

NOVOLOG was not genotoxic in the following tests: Ames test, mouse lymphoma cell forward gene mutation test, human peripheral blood lymphocyte chromosome aberration test, *in vivo* micronucleus test in mice, and in *ex vivo* UDS test in rat liver hepatocytes.

In fertility studies in male and female rats, at subcutaneous doses up to 200 units/kg/day (approximately 32 times the human subcutaneous dose, based on units/body surface area), no direct adverse effects on male and female fertility, or general reproductive performance of animals was observed.

13.2 Animal Toxicology and/or Pharmacology

In standard biological assays in mice and rabbits, one unit of NOVOLOG has the same glucose-lowering effect as one unit of regular human insulin.

14 CLINICAL STUDIES

14.1 Overview of Clinical Studies

The safety and effectiveness of subcutaneous NOVOLOG was compared to regular human insulin in 596 type 1 diabetes adult, 187 pediatric type 1 diabetes, and 91 adult type 2 diabetes patients using NPH as basal insulin (see Tables 3, 4, 5). The reduction in glycated hemoglobin (HbA_{1c}) was similar to regular human insulin.

The safety and effectiveness of NOVOLOG administered by continuous subcutaneous insulin infusion (CSII) by external pump was compared to buffered regular human insulin (administered by CSII), to lispro (administered by CSII) and compared to NOVOLOG injections and NPH injection. Overall, the reduction in HbA_{1c} was similar to the comparator.

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 NOVOLOG to regular human insulin injection in adult patients with type 1 diabetes. 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 15.7 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/m^2.

NOVOLOG was administered by subcutaneous injection immediately prior to meals and regular human insulin was administered by subcutaneous injection 30 minutes before meals. NPH insulin was administered as the basal insulin in either single or divided daily doses. Changes in HbA_{1c} were comparable for the two treatment regimens in this study (Table 3).

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

	NOVOLOG + NPH (N=596)	**Regular Human Insulin+ NPH (N=286)**
Baseline HbA_{1c} (%)*	7.9 ±1.1	8.0 ± 1.2
Change from Baseline HbA_{1c} (%)	-0.1 ± 0.8	0.0 ± 0.8
Treatment Difference in HbA_{1c}, Mean (95% confidence interval)	-0.2 (-0.3, -0.1)	

*Values are Mean ± SD

Type 1 Diabetes – Pediatric (*see* Table 4)

The efficacy of NOVOLOG to improve glycemic control in pediatric patients with type 1 diabetes mellitus is based on an adequate and well-controlled trial of regular human insulin in pediatric patients with type 1 diabetes mellitus (Table 4). This 24-week, parallel-group study of children and adolescents with type 1 diabetes (n = 283), aged 6 to 18 years, compared two subcutaneous multiple-dose treatment regimens: NOVOLOG (n=187) or regular human insulin (n=96). NPH insulin was administered as the basal insulin. Similar effects on HbA_{1c} were observed in both treatment groups (Table 4).

Subcutaneous administration of NOVOLOG and regular human insulin have also been compared in children with type 1 diabetes (n=26) aged 2 to 6 years with similar effects on HbA_{1c}.

Table 4. Pediatric Subcutaneous Administration of NOVOLOG in Type 1 Diabetes (24 weeks; n=283)

	NOVOLOG + NPH (N=187)	**Regular Human Insulin+ NPH (N=96)**
Baseline HbA_{1c} (%)*	8.3 ± 1.2	8.3 ± 1.3
Change from Baseline HbA_{1c} (%)	0.1± 1.0	0.1± 1.1
Treatment Difference in HbA_{1c}, Mean (95% confidence interval)	-0.2 (-0.5, 0.1)	

*Values are Mean ± SD

14.3 Clinical Studies in Adults with Type 2 Diabetes and Subcutaneous Daily Injections

Type 2 Diabetes - Adults (*see* Table 5)

Onesix-month, open-label, active-controlled study was conducted to compare the safety and efficacy of NOVOLOG to regular human insulin in patients with type 2 diabetes (Table 5).

The mean age of the trial population was 56.6 years and mean duration of diabetes was 12.7 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/m^2.

NOVOLOG was administered by subcutaneous injection immediately prior to meals and regular human insulin was administered by subcutaneous injection30 minutes before meals. NPH insulin was administered as the basal insulin in either single or divided daily doses. Changes in HbA_{1c} were comparable for the two treatment regimens.

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

	NOVOLOG + NPH (N=90)	**Regular Human Insulin + NPH (N=86)**
Baseline HbA_{1c} (%)*	8.1 ± 1.2	7.8 ± 1.1
Change from Baseline HbA_{1c} (%)	-0.3 ± 1.0	-0.1 ± 0.8
Treatment Difference in $HbA_{1c,}$ Mean (95% confidence interval)	- 0.1 (-0.4, 0.1)	

*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 – Adult (*see* Table 6)

Two open-label, parallel design studies (6 weeks [n=29] and 16 weeks [n=118]) compared NOVOLOG to buffered 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 HbA_{1c}.

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

	NOVOLOG (N=59)	**Buffered human insulin (N=59)**
Baseline HbA_{1c} (%)*	7.3 ± 0.7	7.5 ± 0.8
Change from Baseline HbA_{1c} (%)	0.0 ± 0.5	0.2 ± 0.6
Treatment Difference in $HbA_{1c,}$ Mean (95% confidence interval)	0.2 (-0.1, 0.4)	

*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=298) aged 4-18 years compared two subcutaneous infusion regimens administered via an external insulin pump: NOVOLOG (n=198) or insulin lispro (n=100). These two treatments resulted in comparable changes from baseline in HbA_{1c} (see Table 7).

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

	NOVOLOG (N=198)	Lispro (N=100)
Baseline HbA_{1c} (%)*	8.0 ± 0.9	8.2 ± 0.8
Change from Baseline HbA_{1c} (%)	-0.1 ± 0.8	-0.1 ± 0.7
Treatment Difference in HbA_{1c}, Mean (95% confidence interval)	-0.1 (-0.3, 0.1)	

*Values are Mean ± SD

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 NOVOLOG injection in conjunction with NPH injections to NOVOLOG 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/m^2.

The two treatment groups had similar reductions in HbA_{1c} (Table 8).

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

	NOVOLOG pump (N=66)	NOVOLOG + NPH (N=61)
Baseline HbA_{1c} (%)*	8.2 ± 1.4	8.0 ± 1.1
Change from Baseline HbA_{1c} (%)	-0.6 ± 1.1	-0.5 ± 0.9
Treatment Difference in HbA_{1c}, Mean (95% confidence interval)	0.1 (-0.3, 0.4)	

*Values are Mean ± SD

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

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

10 mL multiple-dose vial NDC 0169-7501-11
3 mL single-patient-use PenFill cartridges* NDC 0169-3303-12
3 mL single-patient-use NOVOLOG FlexPen NDC 0169-6339-10
3 mL single-patient-use NOVOLOG FlexTouch NDC 0169-6338-10

*NOVOLOG PenFill cartridges are designed for use with Novo Nordisk insulin delivery devices with NovoFine disposable needles. FlexPen and FlexTouch can be used with NovoFine or NovoTwist disposable needles.

The NOVOLOG FlexPen and FlexTouch dial in 1-unit increments.

16.2 Recommended Storage

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

Unused NOVOLOG should be stored in a refrigerator between 2° and 8°C (36° to 46°F). Do not freeze NOVOLOGanddo not use NOVOLOG if it has been frozen. Do not expose NOVOLOG to excessive heat or light.

NOVOLOG should not be drawn into a syringe and stored for later use.

Always remove and discard the needle after each injection from the NOVOLOG FlexPen or NOVOLOG FlexTouchand 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, NOVOLOG FlexPen, and NOVOLOG FlexTouch

NOVOLOG presentation	**Not in-use (unopened)** Room Temperature (below 30°C [86°F])	**Not in-use** (unopened) Refrigerated	**In-use (opened)** Room Temperature (below 30°C [86°F])
10 mL multiple-dose vial	28 days	Until expiration date	28 days (refrigerated/room temperature)
3 mL single-patient-use PenFill cartridges	28 days	Until expiration date	28 days (Do not refrigerate)
3 mL single-patient-use NOVOLOG FlexPen	28 days	Until expiration date	28 days (Do not refrigerate)
3 mL single-patient-use NOVOLOG FlexTouch	28 days	Until expiration date	28 days (Do not refrigerate)

Storage in External Insulin Pump:

NOVOLOG 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 NOVOLOG

NOVOLOG diluted with Insulin Diluting Medium for NOVOLOG to a concentration equivalent to U-10 or 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 NOVOLOG 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 a NOVOLOG FlexPen or a NOVOLOG FlexTouch, PenFill Cartridge or PenFill Cartridge Device between Patients

Advise patients that they must never share NOVOLOG FlexPen, NOVOLOG FlexTouch, 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 NOVOLOG vials not to share needles or syringes with another person. Sharing poses a risk for transmission of blood-borne pathogens *[see Warnings and Precautions (5.1)]*.

Hyperglycemia or Hypoglycemia

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

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

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

Hypoglycemia with Medication Errors

Instruct patients to always check the insulin label before each injection to avoid mix-ups between insulin products *[see Warnings and Precautions (5.3)]*.

Hypersensitivity Reactions

Advise patients that hypersensitivity reactions have occurred with NOVOLOG. Inform patients of the symptoms of hypersensitivity reactions *[see Warnings and Precautions (5.4)]*.

Administration

NOVOLOG must only be used if the solution is clear and colorless with no particles visible. Instruct patients that when injecting NOVOLOG, 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 the frequency of checking their blood glucose and that possible additional insulin administration may be necessary.

If 0 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 selects 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.** NOVOLOG 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 infusion site 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) 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) and How Supplied/Storage and Handling (16.2)]*.

Before using an insulin pump with NOVOLOG, read the pump label to make sure the pump has been evaluated with NOVOLOG.

Rx only

Date of Issue: 11/2019

Version: 27

Novo Nordisk®, NOVOLOG®, PenFill®, Novolin®, FlexPen®, FlexTouch®, NovoFine®, and NovoTwist® are registered trademarks of Novo Nordisk A/S.

Patent Information: http://novonordisk-us.com/patients/products/product-patents.html

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1-800-727-6500

www.novonordisk-us.com

PATIENT INFORMATION

NovoLog® (NŌ-vō-log)

(insulin aspart injection)

Do not share your NovoLog FlexPen, NovoLog FlexTouch, 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 NovoLog?

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

Who should not take NovoLog?

Do not take NovoLog if you:

- are having an episode of low blood sugar (hypoglycemia).
- have an allergy to NovoLog or any of the ingredients in NovoLog.

Before taking NovoLog, 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 NovoLog, talk to your healthcare provider about low blood sugar and how to manage it.

How should I take NovoLog?

- **Read the Instructions for Use** that come with your NovoLog.
- Take NovoLog exactly as your healthcare provider tells you to.
- **NovoLog starts acting fast.** You should eat a meal within 5 to 10 minutes after you take your dose of NovoLog.
- 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.
- NovoLog 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 NovoLog?

While taking NovoLog do not:

- Drive or operate heavy machinery, until you know how NovoLog affects you.
- Drink alcohol or use prescription or over-the-counter medicines that contain alcohol.

What are the possible side effects of NovoLog?

NovoLog 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

- blurred vision
- anxiety, irritability, or mood changes
- sweating
- slurred speech
- hunger
- confusion
- shakiness
- headache
- fast heart beat

Your insulin dose may need to change because of:

- change in level of physical activity or exercise
- increased stress
- change in diet
- weight gain or loss
- illness

Other common side effects of NovoLog 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 NovoLog. 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 NovoLog.

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 NovoLog that is written for health professionals. Do not use NovoLog for a condition for which it was not prescribed. Do not give NovoLog to other people, even if they have the same symptoms that you have. It may harm them.

What are the ingredients in NovoLog?

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

This Patient Information has been approved by the U.S. Food and Drug Administration.

Revised: 11/2019

INSTRUCTIONS FOR USE

NovoLog® (NŌ-vō-log)

(insulin aspart injection)

10 mL multiple-dose vial (100 Units/mL, U-100)

Read this Instructions for Use before you start taking NovoLog 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 NovoLog injection:

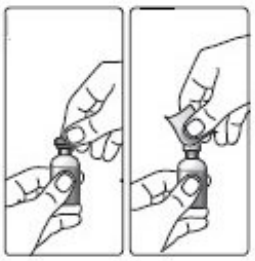
- 10 mL NovoLog vial
- insulin syringe and needle
- alcohol swabs

Preparing your NovoLog dose:

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



(Figure A 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).

(Figure C)

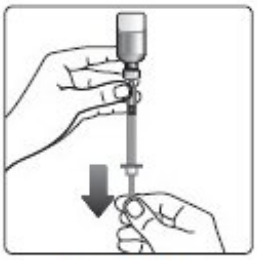
Step 4: Push the needle through the rubber stopper of the NovoLog vial (See Figure D).

(Figure D)

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

(Figure E)

Step 6: Turn the NovoLog 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).



(Figure F)

- If there are air bubbles, tap the syringe gently a few times to let any air bubbles rise to the top (See Figure G).

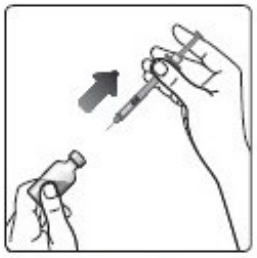
(Figure G)

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

(Figure H)

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

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



(Figure I)

Giving your Injection:

- Inject your NovoLog exactly as your healthcare provider has shown you. Your healthcare provider should tell you if you need to pinch the skin before injecting.
- NovoLogcan 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 NovoLog,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 NovoLog in an insulin pump, you should change your insertion site every 3 days. NovoLog 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 insert into the exact same spot for each insertion. Do not insert where the skin has pits, is thickened, or has lumps. Do not insert 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 NovoLog in an insulin pump, see your insulin pump manual for instructions or talk to your healthcare provider.
- NPH insulin is the only type of insulin that can be mixed with NovoLog. **Do not** mix NovoLog with any other type of insulin.
- NovoLog should **only** be mixed with NPH insulin if it is going to be injected right away under your skin (subcutaneously).
- NovoLog should be drawn up into the syringe **before** you draw up your NPH insulin.
- Talk to your healthcare provider if you are not sure about the right way to mix NovoLog and NPH insulin.

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).

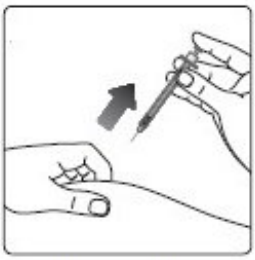
(Figure J)

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.**

(Figure K)

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

- 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 L)

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 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.

How should I store NovoLog?

- **Do not** freeze NovoLog. **Do not** use NovoLog if it has been frozen.
- Keep NovoLog away from heat or light.
- **All unopened vials:**
  - Store unopened NovoLog 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 NovoLogvials 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 NovoLog vials after 28 days, even if they still have insulin left in them.

General information about the safe and effective use of NovoLog

- Always use a new syringe and needle for each injection.
- Do not share syringes or needles.
- Keep NovoLog vials, syringes, and needles out of the reach of children.

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

Manufactured by:

Novo Nordisk A/S

DK-2880 Bagsvaerd, Denmark

NovoLog® is a registered trademark of Novo Nordisk A/S.

Patent Information: http://novonordisk-us.com/patients/products/product-patents.html

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For information about NovoLog contact:

Novo Nordisk Inc.

800 Scudders Mill Road

Plainsboro, New Jersey 08536

1-800-727-6500

www.novonordisk-us.com

Revised: 11/2019

INSTRUCTIONS FOR USE

NovoLog® (NŌ-vō-log) PenFill® 3 mL cartridge 100 Units/mL (U-100)

(insulin aspart injection)

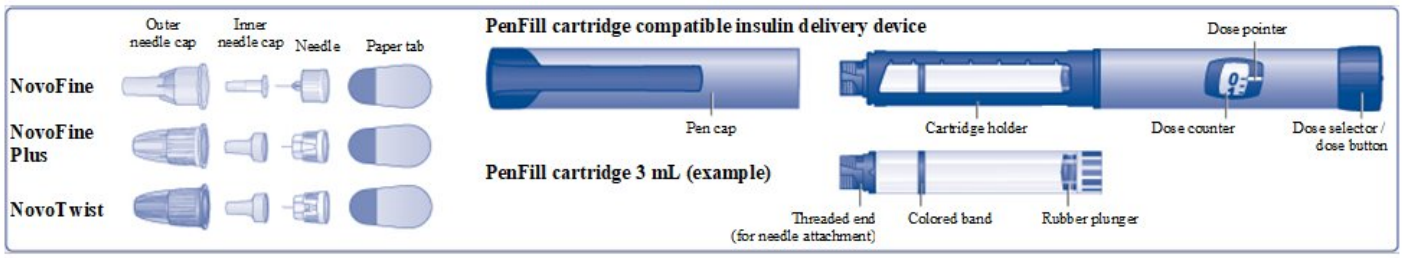
- **Do not share your PenFill cartridge or PenFill cartridge compatible insulin delivery device with other people, even if the needle has been changed. You may give other people a serious infection, or get a serious infection from them.**
- Your healthcare provider should show you or your caregiver how to inject NovoLog the right

way before you inject it for the first time.

- **NovoLog PenFillcartridge 100 Units/mL is a prefilled, single-patient-use cartridge** containing 300 units of NovoLog (insulin aspart injection) 100 Units/mL insulin.
- After you insert the PenFill cartridge in your device, you can use it for multiple injections. Read the **instruction manual** that comes with your insulin delivery device for complete instructions on how to use the PenFill cartridge with the device.
- People who are blind or have vision problems should not use this PenFill cartridge without help from a person trained to use the PenFill cartridge with the device.
- If using a **new** NovoLog PenFill cartridge, start with **Step 1.**
- If the NovoLog PenFill cartridge has already been **used**, start with **Step 2.**

Supplies you will need to give your NovoLog injection:

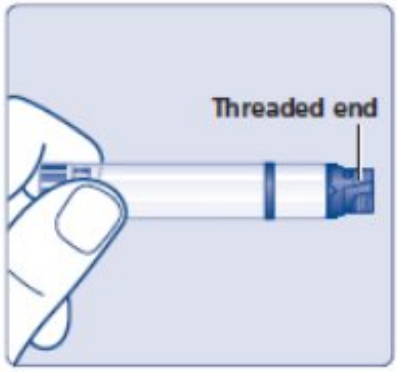
- NovoLog PenFill cartridge
- Novo Nordisk 3 mL PenFill cartridge compatible insulin delivery device
- 1 new NovoFine, NovoFine Plus, or NovoTwist needle
- Alcohol swabs
- Adhesive bandage
- Cotton gauze
- A sharps container for throwing away used PenFill cartridges and needles. **See "After your injection" at the end of these instructions.**



(Figure A)

How to use the NovoLog PenFill cartridge

- Wash your hands with soap and water.
- Before you start to prepare your injection, **check theNovoLogPenFill cartridge label** to make sure that it contains the insulin you need. This is especially important if you take more than 1 type of insulin.
- The tamper-resistant foil should be in place before the first use. If the foil has been broken or removed before your first use of the cartridge, **do not** use it. Call Novo Nordisk at 1-800-727-6500.
- Carefully look at the cartridge and the insulin inside it. Check that the NovoLog cartridge:
    - is not damaged, for example cracked or leaking
    - is not loose on the threaded end
- NovoLog should look clear and colorless. **Do not** use NovoLog if it is cloudy or colored or if the threaded end is loose (See Figure B).



(Figure B)

Step 1:

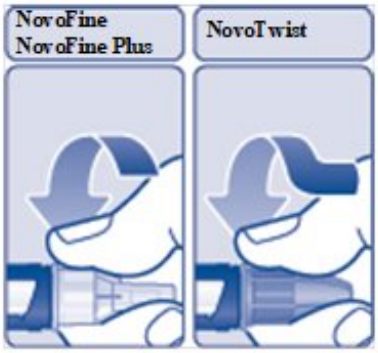
- Insert a 3 mL cartridge with the threaded end first into your Novo Nordisk 3 mL PenFill cartridge compatible insulin delivery device (See Figure C).
- If you drop your device, check the insulin cartridge for damage such as cracks or leaking. If your cartridge is damaged, throw it away and use a new one.

(Figure C)

Prepare your device with a new needle

Step 2:

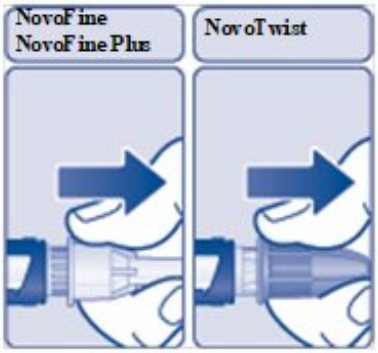
- Take **a new needle,** and tear off the paper tab. Always use a new needle for each injection to make sure the needle is free of germs (sterile) and to prevent blocked needles. **Do not attach a new needle** to your device until you are ready to give your injection. **Do not reuse or share your needles with other people. You may give others a serious infection, or get a serious infection from them**.
- Be careful not to bend or damage the needle before you use it.
- Push the needle straight onto the device. Turn the needle clockwise until it is on tight(See Figure D).



(Figure D)

Step 3:

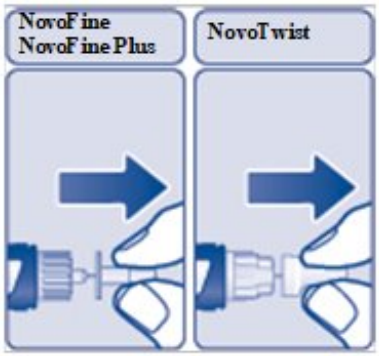
- **Pulloff the outer needle cap** (See Figure E)**. Do not** throw it away. You will need it after the injection to safely remove the needle.



(Figure E)

Step 4:

- **Pulloff the inner needle cap** and throw it away (See Figure F). **Do not** try to put the inner needle cap back on the needle.



(Figure F)

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

Check the insulin flow

Step 5:

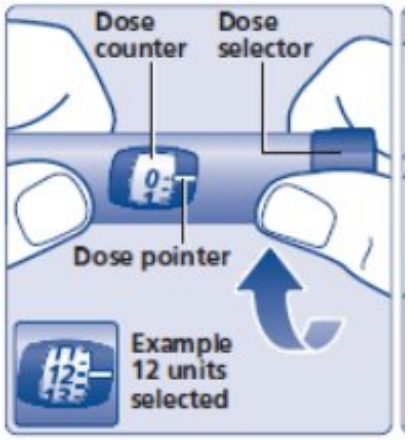
- Small amounts of air may collect in the cartridge during normal use. You must do an airshot before each injection to avoid injecting air and to make sure you receive the prescribed dose of your medicine.
- Do the airshot as described in the instruction manual that comes with your device.
- Keep testing your Novo Nordisk 3 mL PenFill cartridge compatible insulin delivery device until you see insulin at the needle tip. If you still do not see a drop of insulin after 6 times, change the needle and repeat this step. This makes sure that any air bubbles are removed and that insulin is getting through the needle (See Figure G).

(Figure G)

Select your dose

Step 6:

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

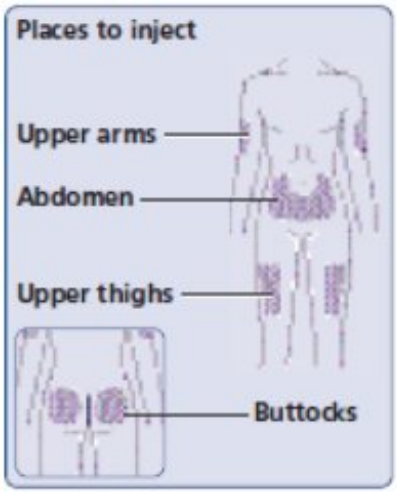


(Figure H)

Inject your dose

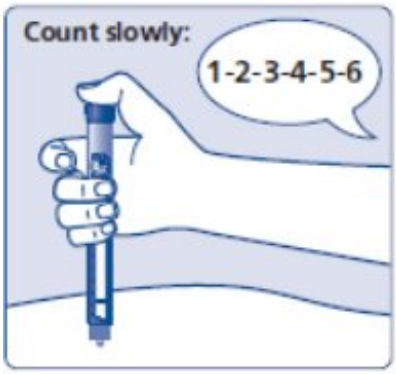
Step 7:

- **Dothe 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.**
- **NovoLog can be injected under the skin (subcutaneously) of your stomach area (abdomen), buttocks, upper legs (thighs), or upper arms (See Figure I).**



(Figure I)

- **Change (rotate) your injection sites within the area you choose for each dose to reduce your risk of getting lipodystrophy (pits in skin or thickened skin) and localized cutaneous amyloidosis (skin with lumps) at the injection sites. Do not use the same injection site for each injection. Do not inject where the skin has pits, is thickened, or has lumps. Do not inject where the skin is tender, bruised, scaly or hard, or into scars or damaged skin.**
- **Cleanyour injection site with an alcohol swab. Let your skin dry. Do not touch this area again before injecting**.
- **Insertthe 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.**



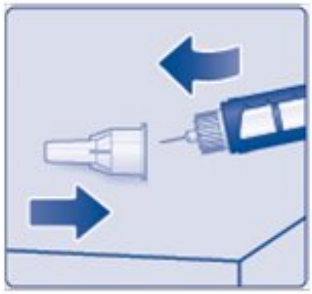
(Figure J)

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

After your injection

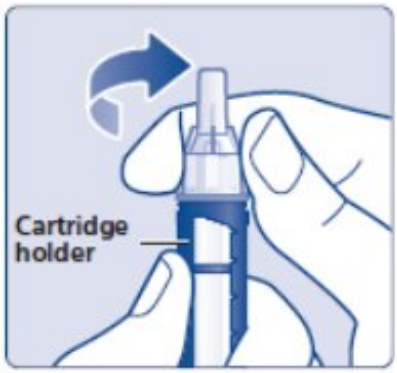
Step 8:

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



(Figure K)

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



(Figure L)

- Throw away (dispose of) the needle in an FDA-cleared sharps container as your healthcare professional has instructed you.
- Put your empty NovoLog PenFill cartridge and used needles in a FDA-cleared sharps disposal container right away after use. Do not throw away (dispose of) loose needles and PenFill cartridges in your household trash.
- If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
    - made of a heavy-duty plastic,
    - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
    - upright and stable during use, and
    - leak-resistant and properly labeled to warn of hazardous waste inside the container.
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or

local laws about how you should throw away used needles and syringes. Do not reuse or share your needles or syringes with other people. For more information about the safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal.

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

Step 9:

- Keep the 3 mL PenFill cartridge in the device. **Do not** store your device with a needle attached. This will prevent infection or leakage of insulin and will make sure that you receive the right dose of NovoLog.
- **Putthe pen cap on** your device after each use to protect the insulin from light (See Figure M).

(Figure M)

How should I store my NovoLog PenFill cartridge?

- **Do not** freeze NovoLog. **Do not** use NovoLog if it has been frozen.
- Keep NovoLog away from heat or light.
- Store the NovoLog PenFill cartridge without the needle attached.

Before use:

- Store unused NovoLog PenFill cartridges in the refrigerator at 36°F to 46°F (2°C to 8°C).
- Unused PenFill cartridges may be used until the expiration date printed on the label, if kept in the refrigerator.
- If NovoLog is stored mistakenly outside of refrigeration between 47°F (9°C) to 86°F (30°C) prior to first use, it should be used within 28 days or thrown away.

PenFill cartridges in use:

- Store the PenFill cartridgeyou 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 NovoLog PenFill cartridge you are using should be thrown away after 28 days, even if it still has insulin left in it.

GeneralInformation about the safe and effective use of NovoLog.

- **Keep NovoLog PenFill cartridges and needles out of the reach of children.**
- **Do not** share NovoLog PenFill cartridgesor needles with other people. You may give other people a serious infection, or get a serious infection from them.

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

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

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Manufactured by:

Novo Nordisk A/S

DK-2880 Bagsvaerd, Denmark

Revised: 11/2019

INSTRUCTIONS FOR USE

NovoLog® (NŌ-vō-log) FlexTouch® Pen

(insulin aspart injection)

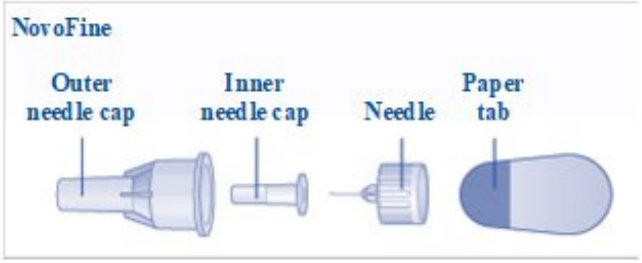
- **Do not share your NovoLog FlexTouch Pen with other people, even if the needle has been is changed. You may give other people a serious infection, or get a serious infection from them.**
- **NovoLog FlexTouch Pen ("Pen") is a prefilled, single-patient-use disposable pen** containing 300 units of U-100 NovoLog (insulin aspart injection) insulin. You can inject from 1 to 80 units in a single injection. The units can be increased by 1 unit at a time.
- **People who are blind or have vision problems should not use this Pen without help from a person trained to use the Pen.**

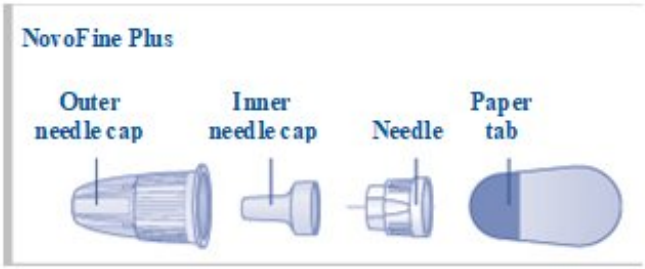
Supplies you will need to give your NovoLog injection:

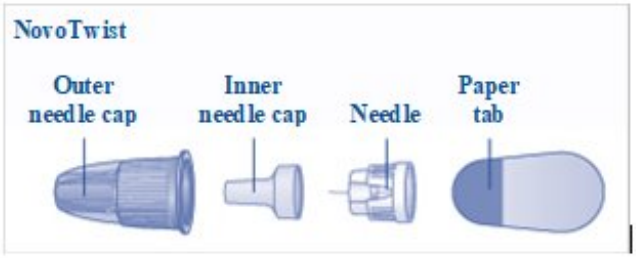
- NovoLog FlexTouch Pen
- a new NovoFine, NovoFine Plus or NovoTwist needle
- alcohol swabs
- 1 sharps container for throwing away used Pens and needles. **See "Disposing of used NovoLog FlexTouch Pens and needles" at the end of these instructions.**

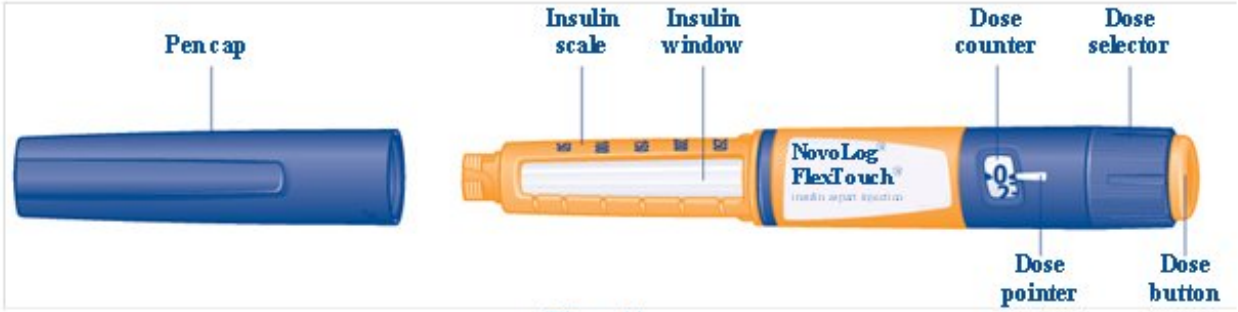
Preparing your NovoLog FlexTouch Pen:

- Wash your hands with soap and water.
- **Before you start to prepare your injection, check the NovoLog FlexTouch Pen label to make sure you are taking the right type of insulin. This is especially important if you take more than 1 type of insulin.**
- NovoLog should look clear and colorless. **Do not** use NovoLog if it is thick, cloudy, or is colored.
- **Do not** use NovoLog past the expiration date printed on the label or 28 days after you start using the Pen.
- **Always** use a new needle for each injection to make sure the needle is free of germs (sterile) and to prevent blocked needles. **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.**





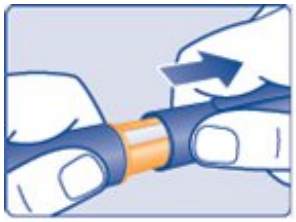




(Figure A)

Step 1:

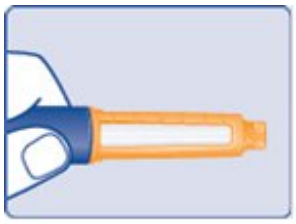
- Pull Pen cap straight off (See Figure B).



(Figure B)

Step 2:

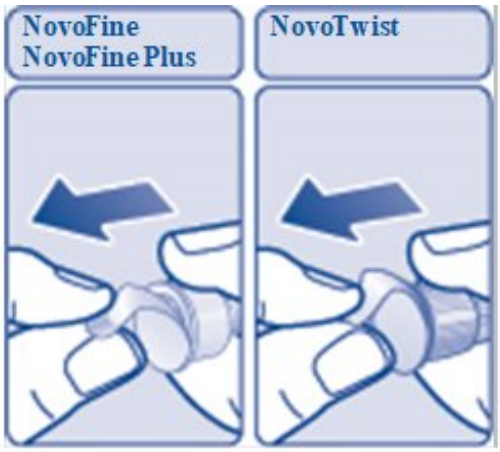
- **Check the liquid in the Pen** (See Figure C). NovoLog should look clear and colorless. **Do not** use it if it looks cloudy or colored.



(Figure C)

Step 3:

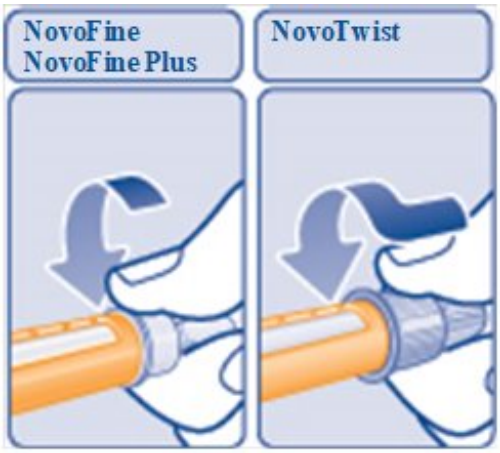
- **Select a new needle.**
- Pull off the paper tab from the outer needle cap (See Figure D).



(Figure D)

Step 4:

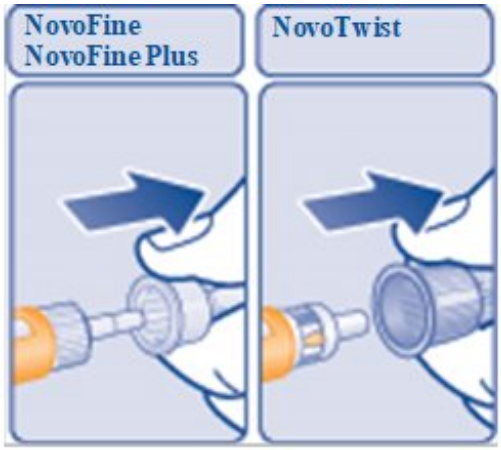
- Push the capped needle straight onto the Pen and twist the needle on until it is tight (See Figure E).



(Figure E)

Step 5:

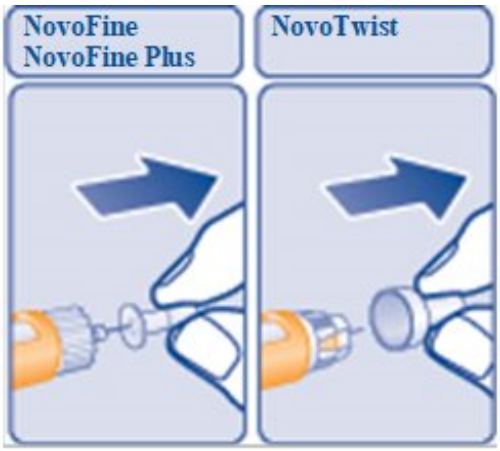
- Pull off the outer needle cap. **Do not** throw it away (See Figure F).



(Figure F)

Step 6:

- Pull off the inner needle cap and throw it away (See Figure G).



(Figure G)

Priming your NovoLog FlexTouch Pen:

Step 7:

- Turn the dose selector to **select 2 units** (See Figure H).

(Figure H)

Step 8:

- Hold the Pen with the needle pointing up. Tap the top of the Pen gently a few times to let any air bubbles rise to the top (See Figure I).

(Figure I)

Step 9:

- **Hold the Pen with the needle pointing up.** Press and hold in the dose button until the dose counter shows “0”. The “0” must line up with the dose pointer.
- A drop of insulin should be seen at the needle tip (See Figure J).
    - If you **do not** see a drop of insulin, repeat steps 7 to 9, no more than 6 times.
    - If you **still do not** see a drop of insulin, change the needle and repeat steps 7 to 9.

(Figure J)

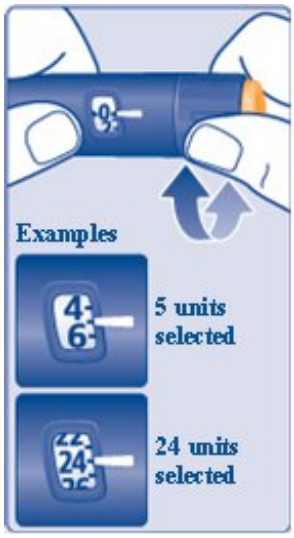
Selecting your dose:

Step 10:

- **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).

- If you select the wrong dose, you can turn the dose selector forwards or backwards to the correct dose.
- The **even** numbers are printed on the dial.
- The **odd** numbers are shown as lines.



(Figure K)

- The NovoLog 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 NovoLog FlexTouch Pen:**

  - 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.
  - 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 NovoLog exactly as your healthcare provider has shown you. Your healthcare provider should tell you if you need to pinch the skin before injecting.
- NovoLog can be injected under the skin (subcutaneously) of your stomach area (abdomen), 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. For each injection, change (rotate) your injection site within the area of skin that you use. **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.

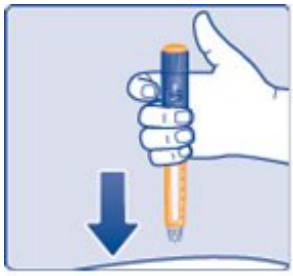
Step 11:

- 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).
    - **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).

- The “0” must line up with the dose pointer. You may then hear or feel a click.

(Figure O)

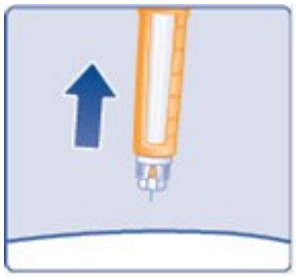
- **Keep the needle in your skin after** the dose counter has returned to “0” and **slowly count to 6** (See Figure P).

(Figure P)

- **When the dose counter returns to “0”, you will not get your full dose until 6 seconds later.**
- **If the needle is removed before you count to 6, you may see a stream of insulin coming from the needle tip.**
- **If you see a stream of insulin coming from the needle tip you will not get your full dose. If this happens you should check your blood sugar levels more often because you may need more insulin.**

Step 14:

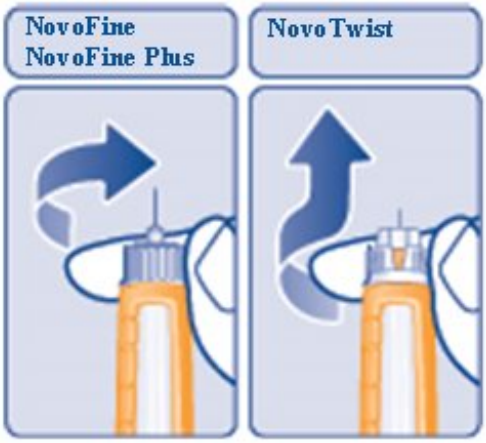
- **Pull the needle out of your skin** (See Figure Q).
  - If you see blood after you take the needle out of your skin, press the injection site lightly with a piece of gauze or an alcohol swab. **Do not** rub the area.



(Figure Q)

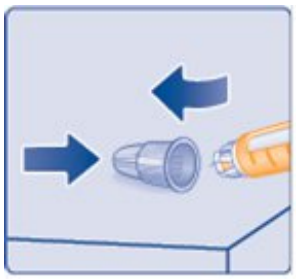
Step 15:

- **Carefully remove the needle from the Pen and throw it away** (See Figure R).
    - **Do not** recap the needle. Recapping the needle can lead to needle stick injury.



(Figure R)

- 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.

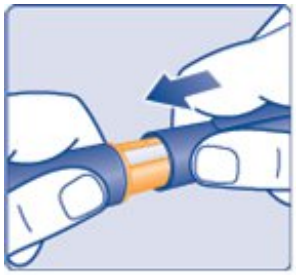


(Figure S)

- **Do not** store the Pen with the needle attached. Storing without the needle attached helps prevent leaking, blocking of the needle, and air from entering the Pen.

Step 16:

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



(Figure T)

After your injection:

- You can put your used NovoLog 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, and
    - leak-resistant and properly labeled to warn of hazardous waste inside the container.
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. Do not reuse or share your needles or syringes with other people. 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 NovoLog FlexTouch Pen?

- **Do not** freeze NovoLog. **Do not** use NovoLog if it has been frozen.
- Keep NovoLog away from heat or light.
- Store the NovoLog FlexTouch Pen without the needle attached.
- **Until first use:**
    - Store unused NovoLog FlexTouch Pens in the refrigerator at 36°F to 46°F (2°C to 8°C).
    - Unused Pens may be used until the expiration date printed on the label, if kept in the refrigerator at 36°F to 46°F (2°C to 8°C).
    - Unused NovoLog FlexTouch Pen stored at room temperature should be thrown away after 28 days.
- **In-use**:
    - Store the Pen you are currently using out of the refrigerator at room temperature below 86°F.
    - The NovoLog FlexTouch Pen 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 NovoLog.

- **Keep NovoLog FlexTouch Pens and needles out of the reach of children.**
- **Always** use a new needle for each injection.
- **Do not share** your NovoLog FlexTouch Pens or needles with other people. You may give other people a serious infection, or get a serious infection from them.

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

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

Revised: 11/2019

For more information go to

www.novotraining.com/novologflextouch/us02

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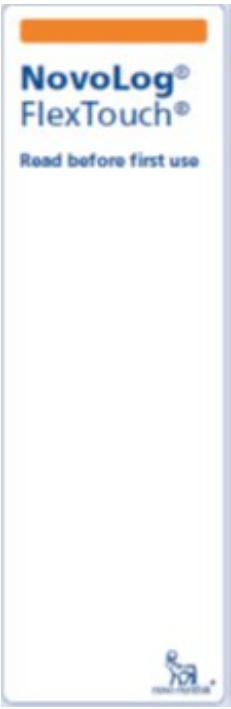


INSTRUCTIONS FOR USE

NovoLog® (NŌ-vō-log) FlexPen®

(insulin aspart injection)

Introduction

Please read the following instructions carefully before using your NovoLog FlexPen.

Do not share your NovoLog 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.

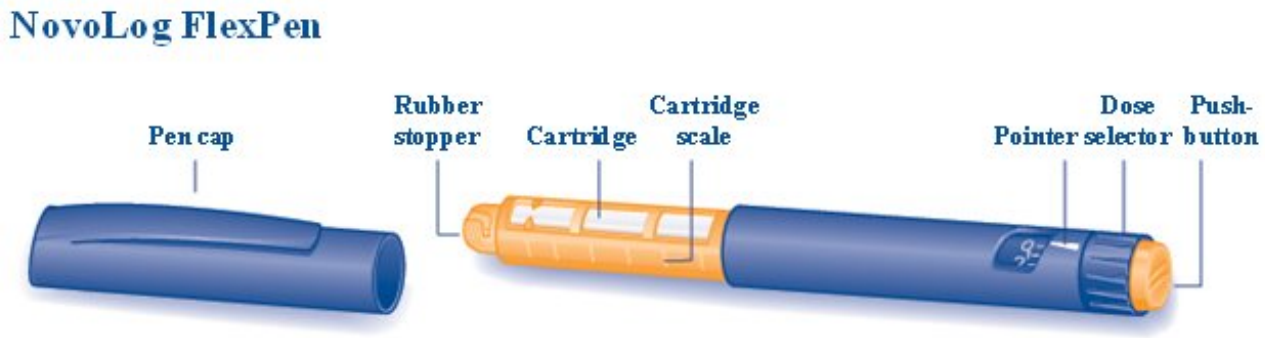
NovoLog FlexPen is a disposable, single-patient-use, dial-a-dose insulin pen. You can select doses from 1 to 60 units in increments of 1 unit. NovoLog FlexPen is designed to be used with NovoFine, NovoFine Plus or NovoTwist needles.

Δ 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:

- NovoLog FlexPen
- New NovoFine, NovoFine Plus or NovoTwist needle
- Alcohol swabs



Preparing your NovoLog 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. NovoLog should look clear and colorless. Do not use your NovoLog FlexPen if the liquid contains particles or is colored.

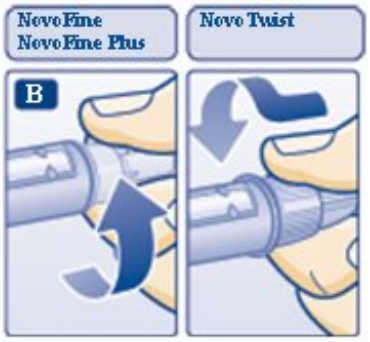
A. Pull off the pen cap (see diagram A).

Wipe the rubber stopper with an alcohol swab.

B. Attaching the needle

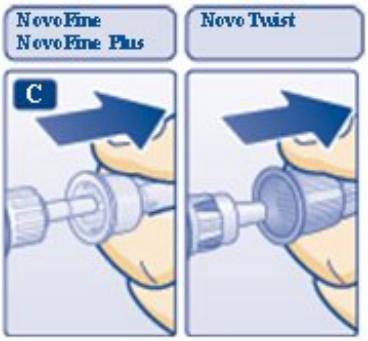
Remove the protective tab from a disposable needle.

Screw the needle tightly onto your FlexPen. It is important that the needle is put on straight (see diagram B).

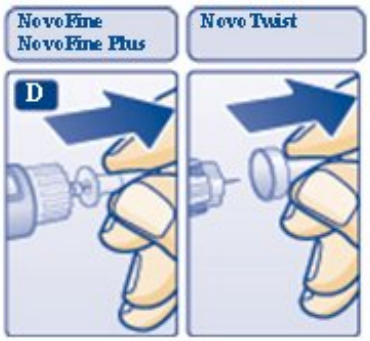


Never place a disposable needle on your NovoLog FlexPen until you are ready to take your injection.

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



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



Δ Always use a new needle for each injection to make sure the needle is free of germs (sterile) and to prevent blocked needles. Do not reuse or share your needles with other people. You may give other people a serious infection, or get a serious infection from them.

Δ Be careful not to bend or damage the needle before use.

Δ To reduce the risk of unexpected needle sticks, **never put the inner needle cap back on the**

needle.

Giving the airshot before each injection

Before each injection small amounts of air may collect in the cartridge during normal use. To avoid injecting air and to ensure proper dosing:

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

F. Hold your NovoLog 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 NovoLog FlexPen and contact Novo Nordisk at 1-800-727-6500.

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.

Δ 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.

NovoLog 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.

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 NovoLog 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 NovoLog FlexPen for your prescribed dose, the NovoLog FlexPen may be thrown away in your household trash after you have removed the needle. The NovoLog FlexPen prevents the cartridge from being completely emptied. It is designed to deliver 300 units.

K. Put the pen cap on the NovoLog FlexPen and store the NovoLog 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.

How should I store NovoLog FlexPen?

- **Do not** freeze NovoLog. **Do not** use NovoLog if it has been frozen.
- Keep NovoLog away from heat or light.
- Store the NovoLog FlexPen without the needle attached.
- **Until first use:**
  - Store unused NovoLog 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 NovoLog 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 NovoLog 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.

Δ Remove the needle from the NovoLog 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.

Δ Be careful when handling used needles to avoid needle sticks and transfer of infectious diseases.

Δ Keep your NovoLog FlexPen and needles out of the reach of children.

Δ Use NovoLog FlexPen as directed to treat your diabetes.

Δ **Do not** share your NovoLog FlexPen or needles with other people. You may give other people a serious infection, or

get a serious infection from them.

Δ Always use a new needle for each injection.

Δ Novo Nordisk is not responsible for harm due to using this insulin pen with products not recommended by Novo

Nordisk.

Δ As a precautionary measure, always carry a spare insulin delivery device in case your NovoLog FlexPen is lost or damaged.

Δ Remember to keep the disposable NovoLog FlexPen with you. Do not leave it in a car or other location where it can get too hot or too cold.

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

Revised: 11/2019

PRINCIPAL DISPLAY PANEL - 10 mL NovoLog Vial

NDC 0169-7501-11

List 750111

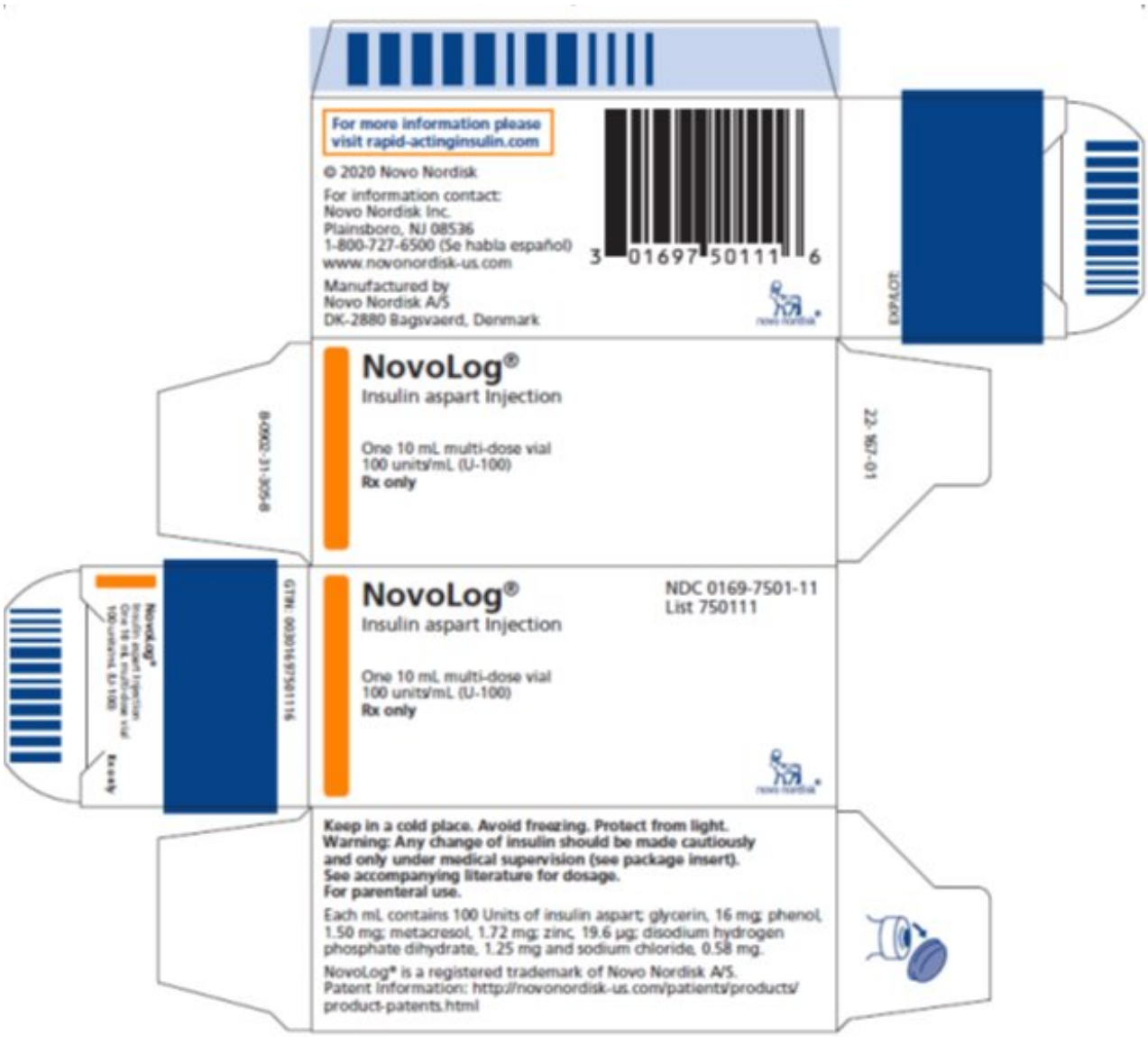
NovoLog®

Insulin aspart Injection

One 10 mL multi-dose vial

100 units/mL (U-100)

Rx only



PRINCIPAL DISPLAY PANEL - 3 mL NovoLog PenFill

NDC 0169-3303-12 List 330312

NovoLog®

PenFill®

Insulin aspart Injection

For Single Patient Use Only

3 mL cartridges

100 units/mL (U-100)

5 cartridges per package

For use with Novo Nordisk 3 mL PenFill® cartridge compatible delivery devices and NovoFine® disposable needles.

Keep in a refrigerator at 36°F to 46°F (2°C to 8°C) until first use. After first use store out of the refrigerator below 86°F (30°C) for up to 28 days.

Avoid freezing.

Protect from light.

Rx only

PRINCIPAL DISPLAY PANEL - 3 mL NovoLog FlexPen

NDC 0169-6339-10 List 633910

NovoLog® FlexPen®

Prefilled Syringe

Insulin aspart Injection

For Single Patient Use Only

100 units/mL (U-100)

5 x 3 mL Prefilled Insulin Syringes

Rx only

For use with NovoFine®, NovoFine® Plus or NovoTwist®

disposable needles.

Keep in a refrigerator at 36ºF to 46ºF (2ºC to 8ºC) until first use. After first use store out of the refrigerator below 86ºF (30ºC) for up to 28 days.

Avoid freezing.

Protect from light.

Dispense in this sealed carton.

PRINCIPAL DISPLAY PANEL - 3 mL NovoLog FlexTouch

NDC 0169-6338-10 List 633810

NovoLog® FlexTouch®

Insulin aspart Injection

For Single Patient Use Only

100 units/mL (U-100)

5 x 3 mL Prefilled Pens

For subcutaneous use only

Rx Only

Recommended for use with NovoFine®, NovoFine® Plus or NovoTwist® disposable needles.

Keep in a refrigerator at 36ºF to 46ºF (2ºC to 8ºC) until first use. After first use store out of the refrigerator below 86ºF (30ºC) for up to 28 days.

Avoid freezing.

Protect from light.

Dispense in this sealed carton.

PRINCIPAL DISPLAY PANEL – Insulin Diluting Medium

List: 200190 NDC 0169-2001-90

Insulin Diluting Medium for NovoLog®

10 mL

Use only with NovoLog®

NOVOLOG

insulin aspart injection, solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0169-7501
Route of Administration	INTRAVENOUS, SUBCUTANEOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
INSULIN ASPART (UNII: D933668QVX) (INSULIN ASPART - UNII:D933668QVX)	INSULIN ASPART	100 [iU] in 1 mL

Inactive Ingredients

Ingredient Name	Strength
SODIUM PHOSPHATE, DIBASIC, DIHYDRATE (UNII: 94255I6E2T)	1.25 mg in 1 mL
GLYCERIN (UNII: PDC6A3C0OX)	16 mg in 1 mL
HYDROCHLORIC ACID (UNII: QTT17582CB)	
METACRESOL (UNII: GGO4Y809LO)	1.72 mg in 1 mL
PHENOL (UNII: 339NCG44TV)	1.5 mg in 1 mL
SODIUM CHLORIDE (UNII: 451W47IQ8X)	0.58 mg in 1 mL

SODIUM HYDROXIDE (UNII: 55X04QC32I)	
ZINC (UNII: J41CSQ7QDS)	19.6 ug in 1 mL

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0169-7501-11	1 in 1 CARTON	08/27/2001	
1		10 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		
2	NDC:0169-7501-90	1 in 1 CARTON	08/27/2001	
2		10 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA020986	08/27/2001	

NOVOLOG

insulin aspart injection, solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0169-3303
Route of Administration	INTRAVENOUS, SUBCUTANEOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
INSULIN ASPART (UNII: D933668QVX) (INSULIN ASPART - UNII:D933668QVX)	INSULIN ASPART	100 [iU] in 1 mL

Inactive Ingredients

Ingredient Name	Strength
SODIUM PHOSPHATE, DIBASIC, DIHYDRATE (UNII: 94255I6E2T)	1.25 mg in 1 mL
GLYCERIN (UNII: PDC6A3C0OX)	16 mg in 1 mL
HYDROCHLORIC ACID (UNII: QTT17582CB)	
METACRESOL (UNII: GGO4Y809LO)	1.72 mg in 1 mL
PHENOL (UNII: 339NCG44TV)	1.5 mg in 1 mL
SODIUM CHLORIDE (UNII: 451W47IQ8X)	0.58 mg in 1 mL
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
ZINC (UNII: J41CSQ7QDS)	19.6 ug in 1 mL

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0169-3303-12	5 in 1 CARTON	08/27/2001	
1		3 mL in 1 CARTRIDGE; Type 0: Not a Combination Product		
2	NDC:0169-3303-91	1 in 1 CARTON	08/27/2001	
2		3 mL in 1 CARTRIDGE; Type 0: Not a Combination Product		
3	NDC:0169-3303-90	5 in 1 CARTON	08/27/2001	
3		3 mL in 1 CARTRIDGE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA020986	08/27/2001	

NOVOLOG

insulin aspart injection, solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0169-6339
Route of Administration	INTRAVENOUS, SUBCUTANEOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
INSULIN ASPART (UNII: D933668QVX) (INSULIN ASPART - UNII:D933668QVX)	INSULIN ASPART	100 [iU] in 1 mL

Inactive Ingredients

Ingredient Name	Strength
SODIUM PHOSPHATE, DIBASIC, DIHYDRATE (UNII: 94255I6E2T)	1.25 mg in 1 mL
GLYCERIN (UNII: PDC6A3C0OX)	16 mg in 1 mL
HYDROCHLORIC ACID (UNII: QTT17582CB)	
METACRESOL (UNII: GGO4Y809LO)	1.72 mg in 1 mL
PHENOL (UNII: 339NCG44TV)	1.5 mg in 1 mL
SODIUM CHLORIDE (UNII: 451W47IQ8X)	0.58 mg in 1 mL
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
ZINC (UNII: J41CSQ7QDS)	19.6 ug in 1 mL

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0169-6339-10	5 in 1 CARTON	01/22/2003	
1		3 mL in 1 SYRINGE, PLASTIC; Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)		
2	NDC:0169-6339-97	1 in 1 CARTON	01/22/2003	08/31/2017

2	NDC:0169-6339-90	3 mL in 1 SYRINGE, PLASTIC; Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)		
3	NDC:0169-6339-98	1 in 1 CARTON	01/22/2003	
3	NDC:0169-6339-90	3 mL in 1 SYRINGE, PLASTIC; Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA020986	01/22/2003	

NOVOLOG

insulin aspart injection, solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0169-6338
Route of Administration	INTRAVENOUS, SUBCUTANEOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
INSULIN ASPART (UNII: D933668QVX) (INSULIN ASPART - UNII:D933668QVX)	INSULIN ASPART	100 [iU] in 1 mL

Inactive Ingredients

Ingredient Name	Strength
SODIUM PHOSPHATE, DIBASIC, DIHYDRATE (UNII: 94255I6E2T)	1.25 mg in 1 mL
GLYCERIN (UNII: PDC6A3C0OX)	16 mg in 1 mL
HYDROCHLORIC ACID (UNII: QTT17582CB)	
METACRESOL (UNII: GGO4Y809LO)	1.72 mg in 1 mL
PHENOL (UNII: 339NCG44TV)	1.5 mg in 1 mL
SODIUM CHLORIDE (UNII: 451W47IQ8X)	0.58 mg in 1 mL
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
ZINC (UNII: J41CSQ7QDS)	19.6 ug in 1 mL

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0169-6338-10	5 in 1 CARTON	10/31/2030	
1		3 mL in 1 SYRINGE, PLASTIC; Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)		
2	NDC:0169-6338-98	1 in 1 CARTON	10/31/2030	
2	NDC:0169-6338-90	3 mL in 1 SYRINGE, PLASTIC; Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA020986	10/31/2013	

INSULIN DILUTING MEDIUM FOR NOVOLOG

water injection injection, solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0169-2001
Route of Administration	INTRAVENOUS, SUBCUTANEOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
WATER (UNII: 059QF0KO0R) (WATER - UNII:059QF0KO0R)	WATER	1 mL in 1 mL

Inactive Ingredients

Ingredient Name	Strength
GLYCERIN (UNII: PDC6A3C0OX)	
SODIUM PHOSPHATE, DIBASIC, DIHYDRATE (UNII: 94255I6E2T)	
METACRESOL (UNII: GGO4Y809LO)	1.5 mg in 1 mL
PHENOL (UNII: 339NCG44TV)	0.65 mg in 1 mL
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0169-2001-90	1 in 1 CARTON	08/01/2018	
1		10 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA020986	08/27/2001	

Labeler - Novo Nordisk (622920320)