NOVOLOG MIX 70/30- insulin aspart injection, suspension
Novo Nordisk Pharmaceutical Industries, LP

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use NOVOLOG MIX 70/30 safely and effectively. See full prescribing information for NOVOLOG MIX 70/30.

NOVOLOG® MIX 70/30 (insulin aspart protamine and insulin aspart) injectable suspension, for subcutaneous use
Initial U.S. Approval: 2001

INDICATIONS AND USAGE

NOVOLOG MIX 70/30 is a mixture of insulin aspart protamine, an intermediate-acting human insulin analog, and insulin aspart, a rapid-acting human insulin analog, indicated to improve glycemic control in adult patients with diabetes mellitus.

Limitations of Use:

- Not recommended for the treatment of diabetic ketoacidosis.
- The proportions of rapid-acting and long-acting insulins are fixed and do not allow for basal versus prandial dose adjustments (1).

DOSAGE AND ADMINISTRATION

- Inspect visually before use. Appearance should be uniformly white and cloudy. Do not use it if it looks clear or if it contains solid particles (2.1).
- NOVOLOG MIX 70/30 must be resuspended immediately before use. Resuspension is easier when the insulin has reached room temperature (2.1).
- Inject NOVOLOG MIX 70/30 subcutaneously in the abdominal region, buttocks, thigh, or upper arm (2.1).
- Administer the dose within 15 minutes before meal initiation. For patients with type 2 diabetes, the dose may also be given after meal initiation (2.1).
- Rotate injection sites within the same region from one injection to the next to reduce risk of lipodystrophy and localized cutaneous amyloidosis (2.1).
- Do not administer intravenously or use in insulin infusion pumps (2.1).
- NOVOLOG MIX 70/30 is typically dosed twice-daily (with each dose intended to cover 2 meals or a meal and a snack) (2.2).
- Individualize dosage based on metabolic needs, blood glucose monitoring results, glycemic control goal (2.2).
- 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 (2.2).
- When switching from another insulin to NOVOLOG MIX 70/30, a different dosage of NOVOLOG MIX 70/30 may be needed (2.2).

DOSAGE FORMS AND STRENGTHS

Injectable suspension: 100 units/mL (U-100) of NOVOLOG MIX 70/30, 70% insulin aspart protamine and 30% insulin aspart available as:

- 10 mL multiple-dose vial (3)
- 3 mL single-patient-use FlexPen prefilled pen (3)

CONTRAINDICATIONS

- Do not use during episodes of hypoglycemia (4).
- Do not use in patients with hypersensitivity to NOVOLOG MIX 70/30 or one of its excipients (4).

WARNINGS AND PRECAUTIONS

- Never share a NOVOLOG MIX 70/30 FlexPen 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, concomitantly 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 MIX 70/30, 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).
- *Fluid retention and heart failure with* concomitant use of *thiazolidinediones (TZDs)*: Observe for signs and symptoms of heart failure; consider dosage reduction or discontinuation if heart failure occurs (5.7).

ADVERSE REACTIONS

Adverse reactions observed with insulin therapy 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, 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 bluntthe signs and symptoms of hypoglycemia:* beta-blockers, clonidine, guanethidine, and reserpine (7).

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

Revised: 2/2023

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

NOVOLOG MIX 70/30 is a mixture of insulin aspart protamine and insulin aspart indicated to improve glycemic control in adult patients with diabetes mellitus.

Limitations of Use:

- NOVOLOG MIX 70/30 is not recommended for the treatment of diabetic ketoacidosis.
- The proportions of rapid-acting and long-acting insulins in NOVOLOG MIX 70/30 are fixed and do not allow for basal versus prandial dose adjustments.

2 DOSAGE AND ADMINISTRATION

2.1 Important Preparation and Administration Instructions

- Always check insulin labels before administration *[see Warnings and Precautions (5.4)]*.
- Inspect NOVOLOG MIX 70/30 visually before use. It should appear uniformly white and cloudy. Do not use it if it looks clear or if it contains solid particles.
- NOVOLOG MIX 70/30 must be resuspended immediately before use. Resuspension is easier when the insulin has reached room temperature.
- When using the:
  - Vial, roll the vial gently in hands in a horizontal position 10 times until the suspension appears uniformly white and cloudy. Inject immediately.
  - NOVOLOG MIX 70/30 FlexPen, roll NOVOLOG MIX 70/30 FlexPen gently between hands in a horizontal position 10 times. Then, turn NOVOLOG MIX 70/30 FlexPen upside down so that the glass ball moves from one end of the reservoir to the other 10 times until the suspension appears uniformly white and cloudy. Inject immediately.
- The NOVOLOG MIX 70/30 FlexPen dials in 1-unit increments.
- Use NOVOLOG MIX 70/30 FlexPen with caution in patients with visual impairment who may rely on audible clicks to dial their dose.
- Inject NOVOLOG MIX 70/30 subcutaneously in the abdominal region, buttocks, thigh, or upper arm.
- Administer the dose within 15 minutes before meal initiation. For patients with type 2 diabetes, the dose may also be given after meal initiation.
- 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)].*
- Do not administer NOVOLOG MIX 70/30 intravenously or use in insulin infusion pumps.
- Do not mix NOVOLOG MIX 70/30 with any other insulins.

2.2 Dosage Recommendations

- NOVOLOG MIX 70/30 is typically dosed twice-daily (with each dose intended to cover 2 meals or a meal and a snack).
- Individualize the dosage of NOVOLOG MIX 70/30 based on the patient'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 (5.3) and Use in Specific Populations (8.6, 8.7)]*.
- When switching from another insulin to NOVOLOG MIX 70/30, a different dosage of NOVOLOG MIX 70/30 may be needed *[see Warnings and Precautions (5.2)]*.
- During changes to a patient’s insulin regimen, increase the frequency of blood glucose monitoring *[see Warnings and Precautions (5.2)].*

2.3 Dosage Modifications for Drug Interactions

Dosage modification may be needed when NOVOLOG MIX 70/30 is used concomitantly with certain drugs *[see Drug Interactions (7)]*.

3 DOSAGE FORMS AND STRENGTHS

Injectable suspension: 100 units/mL (U-100) of NOVOLOG MIX 70/30, 70% insulin aspart protamine and 30% insulin aspart, is a white and cloudy suspension available as:

- 10 mL multiple-dose vial
- 3 mL single-patient-use FlexPen prefilled pen

4 CONTRAINDICATIONS

NOVOLOG MIX 70/30 is contraindicated:

- During episodes of hypoglycemia *[see Warnings and Precautions (5.3)]*
- In patients with hypersensitivity to NOVOLOG MIX 70/30 or one of its excipients *[see Warnings and Precautions (5.5)]*

5 WARNINGS AND PRECAUTIONS

5.1 Never Share NOVOLOG MIX 70/30 FlexPen Between Patients

NOVOLOG MIX 70/30 FlexPen should never be shared between patients, even if the needle is changed. Patients using NOVOLOG MIX 70/30 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 reaction of all insulins, including NOVOLOG MIX 70/30. 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 insulins, the glucose lowering effect time course of NOVOLOG MIX 70/30 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 concomitantly 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 insulin products have been reported. To avoid medication errors between NOVOLOG MIX 70/30 and other insulins, instruct patients to always check the insulin label before each injection.

5.5 Hypersensitivity Reactions

Severe, life-threatening, generalized allergy, including anaphylaxis, can occur with insulins, including NOVOLOG MIX 70/30. If hypersensitivity reactions occur, discontinue NOVOLOG MIX 70/30; treat per standard of care and monitor until symptoms and signs resolve *[see Adverse Reactions (6)].* NOVOLOG MIX 70/30 is contraindicated in patients who have had hypersensitivity reactions to insulin aspart or one of the excipients *[see Contraindications (4)].*

5.6 Hypokalemia

All insulins, including NOVOLOG MIX 70/30, 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 MIX 70/30, 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.

6 ADVERSE REACTIONS

The following adverse reactions are also discussed elsewhere:

- Hypoglycemia *[see Warnings and Precautions (5.3)]*
- Hypoglycemia Due to Medication Errors *[see Warnings and Precautions (5.4)]*
- Hypersensitivity reactions *[see Warnings and Precautions (5.5)]*
- Hypokalemia *[see Warnings and Precautions (5.6)]*

6.1 Clinical Trial Experience

Clinical trials are conducted under widely varying designs, therefore, 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 data in:

- Table 1 reflects the exposure of 55 patients with type 1 diabetes to NOVOLOG MIX 70/30 with a mean exposure duration of three months. The mean age was 43 years old. Sixty-four percent were male and 100% were White. The mean body mass index (BMI) was 26.1 kg/m^2. The mean duration of diabetes was 15 years.
- Table 2 reflects the exposure of 85 patients with type 2 diabetes to NOVOLOG MIX 70/30 with a mean exposure duration of three months. The mean age was 63 years old. Fifty-four percent were male and 100% were White. The mean body mass index (BMI) was 28.1 kg/m^2. The mean duration of diabetes was 15 years.

Common adverse reactions were defined as events that occurred in ≥5%, excluding hypoglycemia, of the population studied. Common adverse reactions that occurred for NOVOLOG MIX 70/30-treated patients with type 1 diabetes mellitus and type 2 diabetes mellitus are listed in Table 1 and Table 2, respectively. The trial was a three-month, open-label trial in patients with type 1 or type 2 diabetes who were treated twice daily (before breakfast and before supper) with NOVOLOG MIX 70/30.

Table 1: Adverse Reactions that Occurred in ≥ 5% of Type 1 Diabetes Mellitus Adult Patients Treated with NOVOLOG MIX 70/30

	NOVOLOG MIX 70/30 (n=55)	
Preferred Term	**N**	**%**
Hypoglycemia	38	69
Headache	19	35
Influenza-like symptoms	7	13
Dyspepsia	5	9

Back pain	4	7
Diarrhea	4	7
Pharyngitis	4	7
Rhinitis	3	5
Skeletal pain	3	5
Upper respiratory tract infection	3	5

Table 2: Adverse Reactions that Occurred in ≥ 5% of Type 2 Diabetes Mellitus Adult Patients Treated with NOVOLOG MIX 70/30

	NOVOLOG MIX 70/30 (n=85)	
Preferred Term	**N**	**%**
Hypoglycemia	40	47
Upper respiratory tract infection	10	12
Headache	8	9
Diarrhea	7	8
Neuropathy	7	8
Pharyngitis	5	6
Abdominal pain	4	5
Rhinitis	4	5

Severe Hypoglycemia

Hypoglycemia is the most commonly observed adverse reaction in patients using insulin, including NOVOLOG MIX 70/30. 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 MIX 70/30 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.

Severe hypoglycemia requiring the assistance of another person and/or parenteral glucose infusion or glucagon administration has been observed in clinical trials with insulin, including trials with NOVOLOG MIX 70/30.

The incidence of severe hypoglycemia in adult patients receiving subcutaneous NOVOLOG MIX 70/30 was 16% and 4% for type 1 and type 2 diabetes patients respectively at 12 weeks *[see Clinical Studies (14)]*.

Allergic Reactions

Patients have experienced reactions such as erythema, edema or pruritus at the site of NOVOLOG MIX 70/30 injection. These reactions usually resolve in a few days to a few weeks, but in some occasions, have required discontinuation of NOVOLOG MIX 70/30. Severe cases of generalized allergy (anaphylaxis) have been reported.

Adverse Reactions Associated with Insulin Initiation and Glucose Control Intensification

Intensification or rapid improvement in glucose control has been associated with 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

Long-term use of insulin, including NOVOLOG MIX 70/30, can cause lipodystrophy at the site of repeated insulin injections. Lipodystrophy includes lipohypertrophy (thickening of adipose tissue) and lipoatrophy (thinning of adipose tissue), and may affect insulin absorption *[see Dosage and Administration (2.1)]*.

Weight Gain

Weight gain can occur with insulins, including NOVOLOG MIX 70/30, and has been attributed to the anabolic effects of insulin and the decrease in glycosuria.

Peripheral Edema

Insulins, including NOVOLOG MIX 70/30, may cause sodium retention and edema, particularly if previously poor metabolic control is improved by intensified insulin therapy.

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 MIX 70/30 in the studies described below with the incidence of antibodies in other studies or to other products may be misleading.

In a 3-month study with an extension in adult patients with type 2 diabetes, 100% of patients who received NOVOLOG MIX 70/30 were positive for anti-insulin antibodies (AIA) at least once during the first 12 months of the study including 91.4% that were positive at baseline. A total of 91.4% of patients who received NOVOLOG MIX 70/30 were positive for anti-drug antibodies (ADA) at least once during the first 12 months of the study, including 62.1% that were positive at baseline.

In a type 2 diabetes clinical trial of NOVOLOG MIX 70/30, initial increase in titers of antibodies to insulin followed by a decrease approaching to baseline values was observed in NOVOLOG MIX 70/30 and Novolin 70/30 treatment groups with similar incidences. These antibodies did not cause deterioration in glycemic control or necessitate increases in insulin dose.

6.3 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of NOVOLOG MIX 70/30. 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 in which other insulins have been accidentally substituted for NOVOLOG MIX 70/30 have been reported.

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

The table below presents clinically significant drug interactions with NOVOLOG MIX 70/30.

Table 3: Clinically Significant Drug Interactions with NOVOLOG MIX 70/30

Drugs that May Increase the Risk of Hypoglycemia	
Drugs:	Antidiabetic agents, ACE inhibitors, angiotensin II receptor blocking agents, disopyramide, fibrates, fluoxetine, monoamine oxidase inhibitors, pentoxifylline, pramlintide, salicylates, somatostatin analog (e.g., octreotide), and sulfonamide antibiotics
Intervention:	Dose adjustment and increased frequency of glucose monitoring may be required when NOVOLOG MIX 70/30 is concomitantly administered with these drugs.
Drugs that May Decrease the Blood Glucose Lowering Effect of NOVOLOG MIX 70/30	
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 MIX 70/30 is concomitantly administered with these drugs.
Drugs that May Increase or Decrease the Blood Glucose Lowering Effect of NOVOLOG MIX 70/30	
Drugs:	Alcohol, beta-blockers, clonidine, and lithium salts. 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 MIX 70/30 is concomitantly 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 MIX 70/30 is concomitantly administered with these drugs.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data with NOVOLOG MIX 70/30 in pregnant women to inform a drug-associated risk for major birth defects and miscarriage. Available information from published randomized controlled trials with insulin aspart use during the second trimester of pregnancy have not 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, still birth, 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 2^{nd} 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 MIX 70/30 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 MIX 70/30, and any potential adverse effects on the breastfed infant from NOVOLOG MIX 70/30, or from the underlying maternal condition.

8.4 Pediatric Use

Safety and effectiveness of NOVOLOG MIX 70/30 have not been established in pediatric patients with diabetes mellitus.

8.5 Geriatric Use

Clinical studies of NOVOLOG MIX 70/30 did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently than younger adult patients. In geriatric patients with diabetes, the initial dosing, dose increments should be conservative to avoid hypoglycemic reactions. Hypoglycemia may be difficult to recognize in geriatric patients.

8.6 Renal Impairment

The effect of renal impairment on the pharmacokinetics of NOVOLOG MIX 70/30 has not been studied. Some studies with human insulin have shown increased circulating levels of insulin in patients with renal failure. Patients with renal impairment may be at increased risk of hypoglycemia and may require more frequent NOVOLOG MIX 70/30 dose adjustment and more frequent blood glucose monitoring *[see Warnings and Precautions (5.3)].*

8.7 Hepatic Impairment

The effect of hepatic impairment on the pharmacokinetics of NOVOLOG MIX 70/30 has not been studied. Patients with hepatic impairment may be at increased risk of hypoglycemia and may require more frequent NOVOLOG MIX 70/30 dose adjustment and more frequent blood glucose monitoring *[see Warnings and Precautions (5.3)].*

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

Insulin aspart protamine and insulin aspart is a human insulin analog containing 70% insulin aspart protamine crystals and 30% soluble insulin aspart. Insulin aspart is homologous with regular human insulin with the exception of a single substitution of the amino acid proline by aspartic acid in position B28, and is produced by recombinant DNA technology utilizing *Saccharomyces cerevisiae* (baker's yeast). Insulin aspart has the empirical formula $C_{256}H_{381}N_{65}O_{79}S_6$ and a molecular weight of 5825.8 Da.

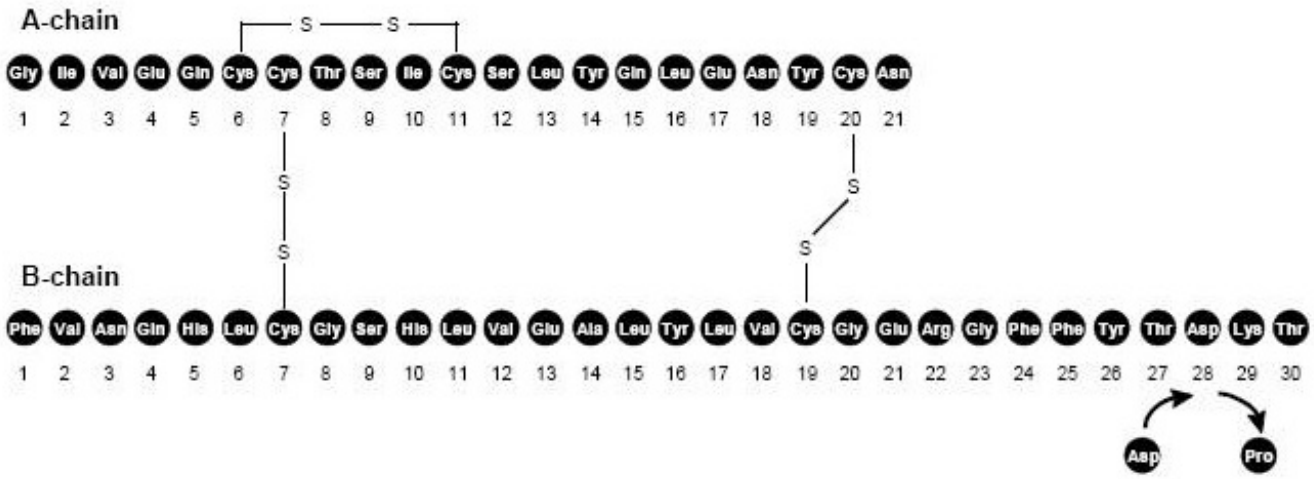


Figure 1. Structural formula of insulin aspart

NOVOLOG MIX 70/30 (insulin aspart protamine and insulin aspart) is a uniform, white and cloudy, sterile injectable suspension for subcutaneous use. Each mL contains 100 units of insulin aspart and the inactive ingredients: disodium hydrogen phosphate dihydrate (1.25 mg), glycerol (16.0 mg), metacresol (1.72 mg), phenol (1.50 mg), protamine sulfate (0.32 mg), sodium chloride (0.877 mg), zinc (19.6 mcg), and Water for Injection, USP. NOVOLOG MIX 70/30 has a pH of 7.20 - 7.44. Hydrochloric acid or sodium hydroxide may be added to adjust pH.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The primary activity of insulin, including NOVOLOG MIX 70/30 is the regulation of glucose metabolism. Insulin and its analog 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

A euglycemic clamp study described below assessed glucose utilization after subcutaneous dosing of NOVOLOG MIX 70/30 in healthy subjects (n = 24). Following a 0.3 units/kg single subcutaneous dose of NOVOLOG MIX 70/30, the onset of action is between 10-20 minutes and the mean ± SD time to peak activity is 2.7 hr ± 0.9 hr. The duration of action may be as long as 24 hours (see Figure 2).

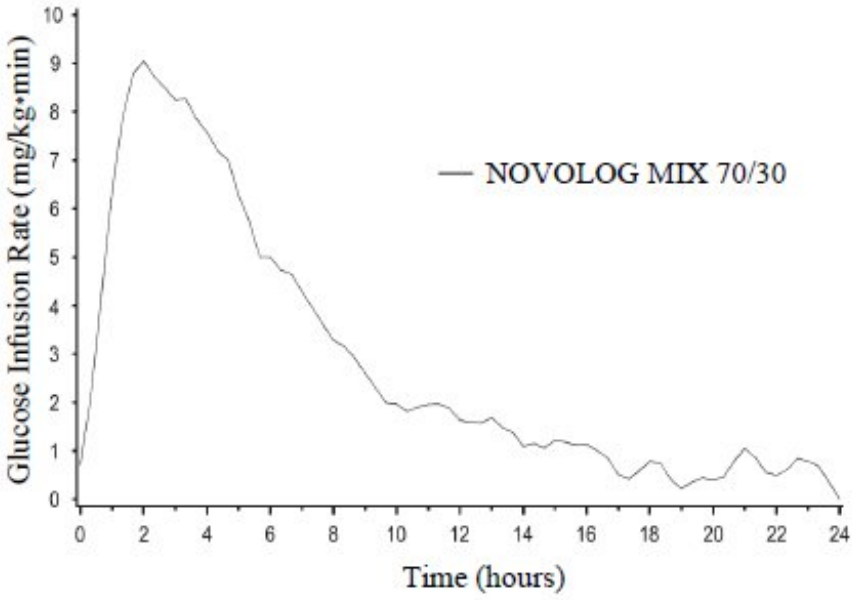


Figure 2. Pharmacodynamic Activity Profile of NOVOLOG MIX 70/30 in healthy subjects after a single 0.3 units/kg subcutaneous dose

12.3 Pharmacokinetics

The single substitution of the amino acid proline with aspartic acid at position B28 in insulin aspart (NOVOLOG) reduces the molecule's tendency to form hexamers as observed with regular human insulin. The rapid absorption characteristics of NOVOLOG are maintained by NOVOLOG MIX 70/30.

Absorption and Bioavailability

The 30% insulin aspart in the soluble component of NOVOLOG MIX 70/30 is absorbed rapidly from the subcutaneous layer. The remaining 70% is in crystalline form as insulin aspart protamine which has a prolonged absorption profile after subcutaneous injection.

The relative bioavailability of NOVOLOG MIX 70/30 compared to NOVOLOG indicates that the insulins are absorbed to similar extent. In a euglycemic clamp study in healthy subjects (n=24) after dosing with NOVOLOG MIX 70/30 (0.3 units/kg), a mean maximum serum concentration (C_{max}) of 61.3 ± 20.1 milliunits/L was reached after 85 minutes.

Serum insulin levels returned to baseline 16 to 20 hours after a subcutaneous dose of NOVOLOG MIX 70/30 (see Fig. 3 for pharmacokinetic profile).

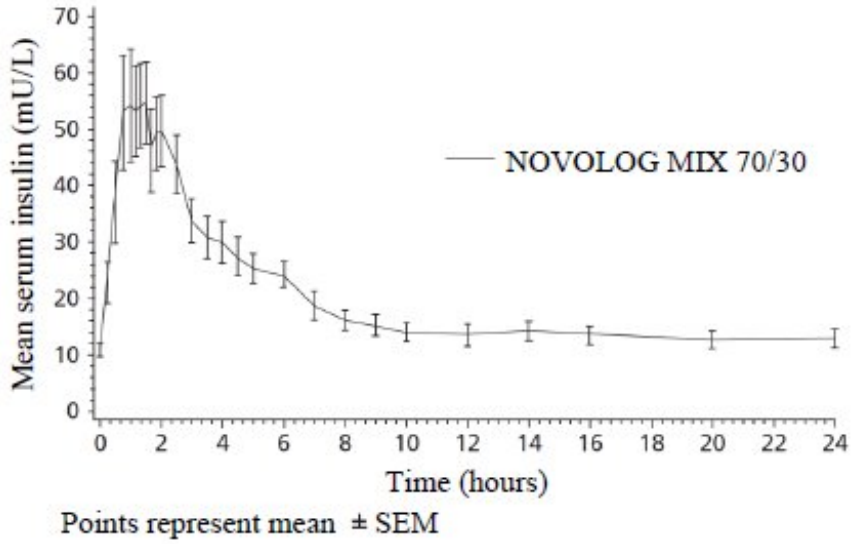


Figure 3. Pharmacokinetic Profile of NOVOLOG MIX 70/30 after a single 0.3 units/kg subcutaneous dose

Distribution and Elimination

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

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 MIX 70/30. In 52-week studies, Sprague-Dawley rats were dosed subcutaneously with NOVOLOG, the rapid-acting component of NOVOLOG MIX 70/30, at 10, 50, and 200 units/kg/day (approximately 2, 8, and 32 times the human subcutaneous dose of 1.0 unit/kg/day, based on units/body surface area, respectively). At a dose of 200 units/kg/day, NOVOLOG increased the incidence of mammary gland tumors in females when compared to untreated controls. The relevance of these findings to humans is not known.

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

14 CLINICAL STUDIES

14.1 Clinical Studies in Adult Patients with Type 1 and Type 2 Diabetes

In a three-month, open-label trial, adult patients with type 1 (n=104) or type 2 (n=187) diabetes mellitus were treated twice daily (before breakfast and before supper) with NOVOLOG MIX 70/30 or Novolin 70/30. Patients had received insulin for at least 24 months before the study. Oral hypoglycemic agents were not allowed within 1 month prior to the study or during the study. The small changes in HbA_{1c} were comparable across the treatment groups (see Table 4).

For patients with type 1 diabetes mellitus (T1DM) the mean age was 43 years old, 64% were male, 100% were White, the mean body mass index (BMI) was 26.1 kg/m^2, and mean duration of diabetes mellitus was 15 years. For patients with type 2 diabetes mellitus (T2DM), the mean age was 63 years old, 54% were male, 100% were White, the BMI 28.1 kg/m^2, and the mean duration of diabetes mellitus was 15 years.

Table 4: Glycemic Parameters at the End of Treatment [Mean ± SD (n subjects)]

	NOVOLOG MIX 70/30	**Novolin 70/30**
Type 1, n=104		
Fasting Blood Glucose (mg/dL)	174 ± 64 (48)	142 ± 59 (44)
1.5 Hour Post Breakfast (mg/dL)	187 ± 82 (48)	200 ± 82 (42)
1.5 Hour Post Dinner (mg/dL)	162 ± 77 (47)	171 ± 66 (41)
HbA_{1c} (%) Baseline	8.4 ± 1.2 (51)	8.5 ± 1.1 (46)
HbA_{1c} (%) Week 12	8.4 ± 1.1 (51)	8.3 ± 1.0 (47)
Type 2, n=187		
Fasting Blood Glucose (mg/dL)	153 ± 40 (76)	152 ± 69 (93)
1.5 Hour Post Breakfast (mg/dL)	182 ± 65 (75)	200 ± 80 (92)
1.5 Hour Post Dinner (mg/dL)	168 ± 51 (75)	191 ± 65 (93)
HbA_{1c} (%) Baseline	8.1 ± 1.2 (82)	8.2 ± 1.3 (98)
HbA_{1c} (%) Week 12	7.9 ± 1.0 (81)	8.1 ± 1.1 (96)

The significance, with respect to the long-term clinical sequelae of diabetes, of the differences in postprandial hyperglycemia between treatment groups has not been established.

14.2 Clinical Studies in Adult Patients with Type 2 Diabetes with Insulin and Oral Antidiabetic Agents

Trial 1:

In a 34-week, open-label trial (Trial 1), insulin-naïve patients with type 2 diabetes mellitus currently treated with 2 oral antidiabetic agents were switched to treatment with metformin and pioglitazone. The mean age of the trial population was 53 years and mean duration of diabetes was 9.2 years. Forty-six percent were male. Eighty-five percent were White, 12% were Black and 3% were Asian. The mean BMI was approximately 32.4 kg/m^2. During an 8-week optimization period metformin and

pioglitazone were increased to 2,500 mg per day and 30 or 45 mg per day, respectively. After the optimization period, patients were randomized to receive either NOVOLOG MIX 70/30 twice daily added on to the metformin and pioglitazone regimen or continue the current optimized metformin and pioglitazone therapy. NOVOLOG MIX 70/30 was started at a dose of 6 international units twice daily (before breakfast and before supper). Insulin doses were titrated to a pre-meal glucose goal of 80-110 mg/dL. The total daily insulin dose at the end of the study was 56.9 ± 30.5 international units.

Table 5: Combination Therapy with Metformin and Pioglitazone in Patients with Type 2 Diabetes Mellitus [Mean (SD)] (Trial 1)

Treatment duration 24-weeks	**NOVOLOG MIX 70/30 + Metformin + Pioglitazone**	**Metformin + Pioglitazone**
HbA_{1c}		
Baseline mean ± SD (n)	8.1 ± 1.0 (102)	8.1 ± 1.0 (98)
End-of-study mean ± SD (n) - LOCF	6.6 ± 1.0 (93)	7.8 ± 1.2 (87)
Adjusted Mean change from baseline ± SE (n)*	-1.6 ± 0.1 (93)	-0.3 ± 0.1 (87)
Treatment difference mean ± SE* 95% CI*	-1.3 ± 0.1 (-1.6, -1.0)	
Percentage of subjects reaching HbA_{1c} <7.0%	76%	24%
Percentage of subjects reaching HbA_{1c} ≤6.5%	59%	12%
Fasting Blood Glucose (mg/dL)		
Baseline Mean ± SD (n)	173 ± 39.8 (93)	163 ± 35.4 (88)
End of Study Mean ± SD (n) - LOCF	130 ± 50.0 (90)	162 ± 40.8 (84)
Adjusted Mean change from baseline ± SE (n)*	-43.0 ± 5.3 (90)	-3.9 ± 5.3 (84)
End-of-Study Blood Glucose (Plasma) (mg/dL)		
2 Hour Post Breakfast	138 ± 42.8 (86)	188 ± 57.7 (74)
2 Hour Post Lunch	150 ± 41.5 (86)	176 ± 56.5 (74)
2 Hour Post Dinner	141 ± 57.8 (86)	195 ± 60.1 (74)

*Adjusted mean per group, treatment difference, and 95% CI were obtained based on an ANCOVA model with treatment, FPG stratum, and secretagogue stratum as fixed factors and baseline HbA_{1c} as the covariate.

Trial 2:

In a 28-week, open-label trial (Trial 2), insulin-naïve patients with type 2 diabetes with fasting plasma glucose above 140 mg/dL currently treated with metformin ± thiazolidinedione therapy were randomized to receive either NOVOLOG MIX 70/30 twice daily [before breakfast and before supper] or insulin glargine once daily (see Table 6). NOVOLOG MIX 70/30 was started at an average dose of 5-6 international units (0.07 ± 0.03 international units/kg) twice daily (before breakfast and before supper), and bedtime insulin glargine was started at 10-12 international units (0.13 ± 0.03 international units/kg). Insulin doses were titrated weekly by decrements or increments of -2 to +6 units per injection to a pre-meal glucose goal of 80-110 mg/dL. The metformin dose was adjusted to 2,550 mg/day. Approximately one-third of the patients in each group were also treated with pioglitazone (30 mg/day). Insulin secretagogues were discontinued in order to reduce the risk of

hypoglycemia. Most patients were White (53%), and the mean initial weight was 90 kg.
The mean age of the trial population was 53 years old and mean duration of diabetes was 9.5 years. Fifty three percent were male. Fifty-five percent were White, 15% Black, 27% were Hispanic, 2% were Asian and 2% were Other. The mean BMI was approximately 31.5 kg/m^2.

Table 6:Combination Therapy with Metformin ± Pioglitazone and Two Types of Insulin in Patients with Type 2 Diabetes Mellitus [Mean (SD)] (Trial 2)

Treatment duration 28-weeks	**NOVOLOG MIX 70/30 + Metformin ± Pioglitazone**	**Insulin Glargine + Metformin ± Pioglitazone**
Number of patients	117	116
HbA_{1c}		
Baseline mean (%)	9.7 ± 1.5 (117)	9.8 ± 1.4 (114)
End-of-study mean (± SD)	6.9 ± 1.2 (108)	7.4 ± 1.2 (114)
Mean change from baseline	-2.7 ± 1.6 (108)	-2.4 ± 1.5 (114)
Percentage of subjects reaching HbA_{1c} <7.0%	66%	40%

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

NOVOLOG MIX 70/30 (insulin aspart protamine and insulin aspart) is a white and cloudy injectable suspension containing 100 units/mL (U-100) of 70% insulin aspart protamine and 30% insulin aspart available as:

One 10 mL multiple-dose vial per carton		NDC 0169-3685-12
	ReliOn® brand	NDC 0169-2200-11
Five 3 mL single-patient-use FlexPen prefilled pens per carton		NDC 0169-3696-19
	ReliOn® brand	NDC 0169-2201-25

The NOVOLOG MIX 70/30 FlexPen dials in 1-unit increments.

16.2 Recommended Storage

Dispense in the original sealed carton with the enclosed Instructions for Use. Store unused NOVOLOG MIX 70/30 in a refrigerator between 2°C to 8°C (36°F to 46°F). Do not freeze NOVOLOG MIX 70/30 or use NOVOLOG MIX 70/30 if it has been frozen. Do not expose NOVOLOG MIX 70/30 to excessive heat or light.

Always remove the needle after each injection and store NOVOLOG MIX 70/30 FlexPen without a needle attached.

The storage conditions are summarized in the following table:

Table 7: Storage conditions for NOVOLOG MIX 70/30 vial and FlexPen

	Not in-use (unopened) Room Temperature (up to 30°C [86°F])	Not in-use (unopened) Refrigerated (2°C to 8°C [36°F to 46°F])	In-use (opened) Room Temperature (up to 30°C [86°F])
10 mL multiple-dose vial	**28 days**	**Until expiration date**	**28 days (refrigerated/room temperature)**
3 mL single-patient-use FlexPen	**14 days**	**Until expiration date**	**14 days (Do not refrigerate)**

17 PATIENT COUNSELING INFORMATION

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

Never Share a NOVOLOG MIX 70/30 FlexPen between Patients

Advise patients that they must never share NOVOLOG MIX 70/30 FlexPen device with another person even if the needle is changed. Advise patients using NOVOLOG MIX 70/30 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 MIX 70/30 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 (5.4)]*.

Hypersensitivity Reactions

Advise patients that hypersensitivity reactions have occurred with NOVOLOG MIX 70/30.

Inform patients of the symptoms of hypersensitivity reactions *[see Warnings and Precautions (5.5)]*.

Manufactured by:

Novo Nordisk Inc.

800 Scudders Mill Road

Plainsboro, NJ 08536

U.S. License Number 1261

Version: 18

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ReliOn® is a registered trademark of Walmart Inc. and is used under license by Novo Nordisk Inc.

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

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For additional information about NOVOLOG MIX 70/30 contact:

Novo Nordisk Inc.

800 Scudders Mill Road

Plainsboro, NJ 08536

1-800-727-6500

(Se Habla español)

www.novonordisk-us.com

PATIENT INFORMATION

NovoLog® Mix 70/30 (NŌ-vō-log-MIX-SEV-en-tee-THIR-tee)
(insulin aspart protamine and insulin aspart)
injectable suspension, for subcutaneous use

Do not share your NovoLog Mix 70/30 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.

What is NovoLog Mix 70/30?

- NovoLog Mix 70/30 is a man-made insulin that is used to control high blood sugar in people with diabetes mellitus.
- It is not known if NovoLog Mix 70/30 is safe and effective in children.

Who should not take NovoLog Mix 70/30?
Do not take NovoLog Mix 70/30 if you:

- are having an episode of low blood sugar (hypoglycemia).

- have an allergy to NovoLog Mix 70/30 or any of the ingredients in NovoLog Mix 70/30.

Before taking NovoLog Mix 70/30, 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 Mix 70/30, talk to your healthcare provider about low blood sugar and how to manage it.

How should I take NovoLog Mix 70/30?

- **Read the Instructions for Use** that come with your NovoLog Mix 70/30.
- Take NovoLog Mix 70/30 exactly as your healthcare provider tells you to.
- **NovoLog Mix 70/30 starts acting fast. If you have Type 1 diabetes, inject it up to 15 minutes before you eat a meal.** Do not inject NovoLog Mix 70/30 if you are not planning to eat within 15 minutes. **If you have Type 2 diabetes, you may inject NovoLog Mix 70/30 up to 15 minutes before or after starting your meal.**
- **Do not mix** NovoLog Mix 70/30 with other insulin products **or** use in an insulin pump.
- 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 or syringes with other people.** You may give other people a serious infection or get a serious infection from them.
- NovoLog Mix 70/30 is injected under the skin (subcutaneously) of your stomach area, buttocks, upper legs, or upper arms.
- **Change (rotate) your injection sites within the same 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 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 Mix 70/30?
While taking NovoLog Mix 70/30 do not:

- Drive or operate heavy machinery, until you know how NovoLog Mix 70/30 affects you.
- Drink alcohol or use prescription or over-the-counter medicines that contain alcohol.

What are the possible side effects of NovoLog Mix 70/30?
NovoLog Mix 70/30 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 Mix 70/30 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 Mix 70/30. 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 Mix 70/30.
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 Mix 70/30 that is written for health professionals. Do not use NovoLog Mix 70/30 for a condition for which it was not prescribed. Do not give NovoLog Mix 70/30 to other people, even if they have the same symptoms that you have. It may harm them.

What are the ingredients in NovoLog Mix 70/30?
Active Ingredient: 70% insulin aspart protamine and 30% insulin aspart.
Inactive Ingredients: disodium hydrogen phosphate dihydrate, glycerol, metacresol, phenol, protamine sulfate, sodium chloride, zinc, and Water for Injection, USP. Hydrochloric acid or sodium hydroxide may be added to adjust pH.

Manufactured by: Novo Nordisk Inc., Plainsboro, NJ 08536 U.S. License Number 1261
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: 2/2023

INSTRUCTIONS FOR USE

NovoLog® Mix 70/30

(insulin aspart protamine and insulin aspart)

injectable suspension, for subcutaneous use

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

Read this Instructions for Use before you start taking NovoLog Mix 70/30 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 Mix 70/30 injection:

- 10 mL NovoLog Mix 70/30 vial
- insulin syringe and needle
- alcohol swabs



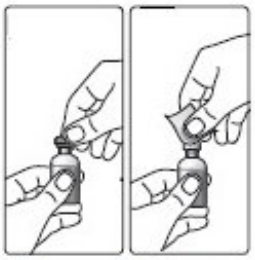
Preparing your NovoLog Mix 70/30 dose:

- Wash your hands with soap and water.
- Before you start to prepare your injection, check the NovoLog Mix 70/30 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 Mix 70/30 should look white and cloudy after mixing. **Do not** use NovoLog Mix 70/30 if it looks clear or contains any lumps or particles.
- NovoLog Mix 70/30 is easier to mix when it is at room temperature.
- After mixing NovoLog Mix 70/30, inject your dose right away. If you wait to inject your dose, the insulin will need to be mixed again.
- **Do not** use NovoLog Mix 70/30 past the expiration date printed on the label.



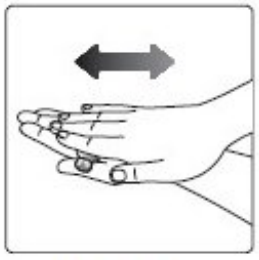
Step 1: If you are using a new vial, pull off the tamper-resistant cap (See Figure A).

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



(Figure A Figure B)

Step 3: Roll the NovoLog Mix 70/30 vial between your hands 10 times. Keep the vial in a horizontal (flat) position (See Figure C). Roll the vial between your hands until the NovoLog Mix 70/30 looks white and cloudy. **Do not shake the vial.**



(Figure C)

Step 4: 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 D).



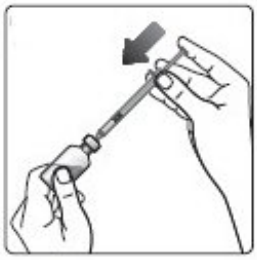
(Figure D)

Step 5: Push the needle through the rubber stopper of the NovoLog Mix 70/30 vial (See Figure E).



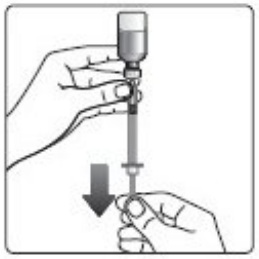
(Figure E)

Step 6: Push the plunger all the way in. This puts air into the NovoLog Mix 70/30 vial (See Figure F).



(Figure F)

Step 7: Turn the NovoLog Mix 70/30 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 G).



(Figure G)

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



(Figure H)

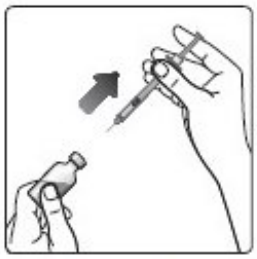
Step 8: Slowly push the plunger up until the black tip reaches the line for your NovoLog Mix 70/30 dose (See Figure I).



(Figure I)

Step 9: Check the syringe to make sure you have the right dose of NovoLog Mix 70/30.

Step 10: Pull the syringe out of the vial's rubber stopper (See Figure J).



(Figure J)

Giving your injection:

- Inject your NovoLog Mix 70/30 exactly as your healthcare provider has shown you. Your healthcare provider should tell you if you need to pinch the skin before injecting.
- NovoLog Mix 70/30 is injected under the skin (subcutaneously) of your stomach area, buttocks, upper legs, 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, 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 K).



(Figure K)

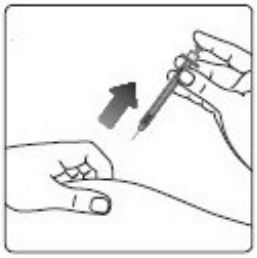
Step 12: Insert the needle into your skin. Push down on the plunger to inject your dose (See Figure L). The needle should remain in the skin for at least 6 seconds to make sure you have injected all the insulin.



(Figure L)

Step 13: Pull the needle out of your skin. After that, you may see a drop of NovoLog Mix 70/30 at the needle tip. This is normal and does not affect the dose you just received (See Figure M).

- 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 M)

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 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 Mix 70/30?

- **Do not** freeze NovoLog Mix 70/30. **Do not** use NovoLog Mix 70/30 if it has been frozen.
- Keep NovoLog Mix 70/30 away from heat or light.

All unopened vials:

- Store unopened NovoLog Mix 70/30 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 NovoLog Mix 70/30 vials can be stored in the refrigerator 36°F to 46°F (2°C to 8°C) or at room temperature below 86°F (30°C) for up to 28 days.
- Throw away all opened NovoLog Mix 70/30 vials after 28 days, even if they still have insulin left in them.

General information about the safe and effective use of NovoLog Mix 70/30

- Always use a new syringe and needle for each injection.
- Do not share syringes or needles.
- Keep NovoLog Mix 70/30 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 Inc.

800 Scudders Mill Road

Plainsboro, New Jersey 08536

1-800-727-6500

U.S. License Number 1261

Revised: 2/2023

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

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

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For information about NovoLog Mix 70/30 contact:

Novo Nordisk Inc.

800 Scudders Mill Road

Plainsboro, New Jersey 08536

1-800-727-6500

www.novonordisk-us.com

INSTRUCTIONS FOR USE

NovoLog® Mix 70/30 FlexPen®

(insulin aspart protamine and insulin aspart)

injectable suspension, for subcutaneous use

FlexPen®

Read the following instructions carefully before you start using your NovoLog Mix 70/30 FlexPen and each time you get a refill. There may be new information. You should read the instructions even if you have used NovoLog Mix 70/30 FlexPen before.

Do not share your NovoLog Mix 70/30 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.

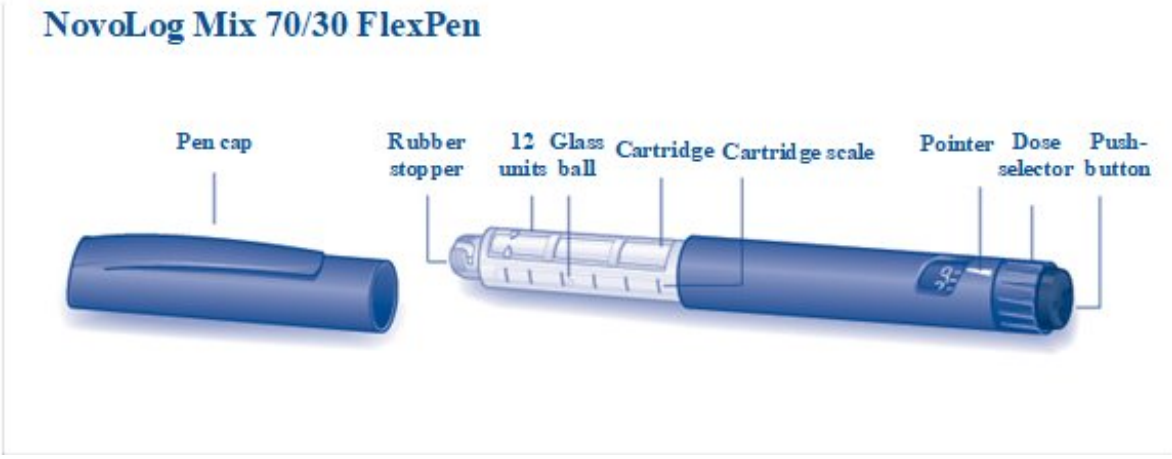
NovoLog Mix 70/30 FlexPen is a disposable, single-patient-use dial-a-dose insulin pen. You can select doses from 1 to 60 units in increments of 1 unit. NovoLog Mix 70/30 FlexPen is designed to be used with NovoFine, NovoFine Plus or NovoTwist needles.

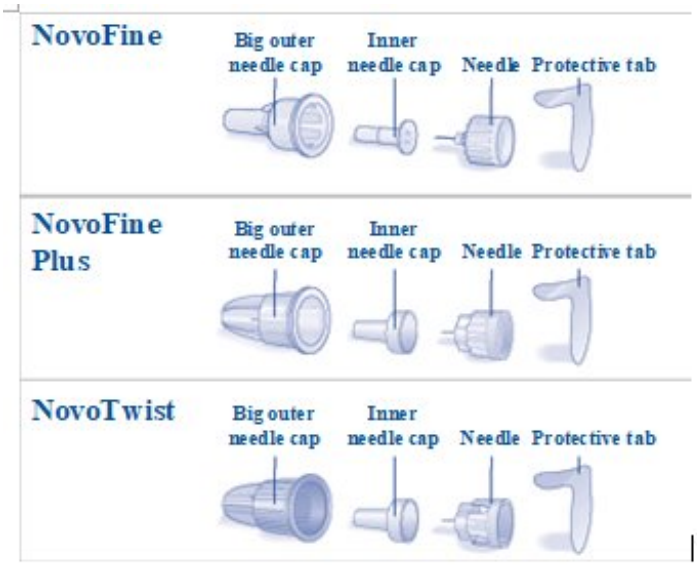
People who are blind or have vision problems should not use NovoLog Mix 70/30 FlexPen without help from a person trained to use NovoLog Mix 70/30 FlexPen.

Getting ready

Make sure you have the following items:

- NovoLog Mix 70/30 FlexPen
- New NovoFine, NovoFine Plus or NovoTwist needle
- Alcohol swabs





Preparing your NovoLog Mix 70/30 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 Mix 70/30 should look cloudy after mixing.

Before your first injection with a new NovoLog Mix 70/30 FlexPen you must mix the insulin:

A. Let the insulin reach room temperature before you use it. This makes it easier to mix.

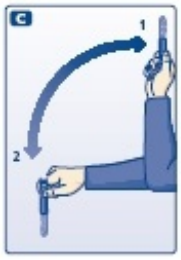
Pull off the pen cap (see diagram A).



B. Roll the pen between your palms 10 times - it is important that the pen is kept horizontal (see diagram B).



C. Then gently move the pen up and down ten times between position **1** and **2** as shown, so the glass ball moves from one end of the cartridge to the other (see diagram C).



Repeat rolling and moving the pen until the liquid appears white and cloudy. Do not use the pen if the liquid appears discolored or contains particles.

For every following injection move the pen up and down between positions 1 and 2 at least ten times until the liquid appears white and cloudy.

After mixing, complete all the following steps of the injection right away. If there is a delay, the insulin will need to be mixed again.

Wipe the rubber stopper with an alcohol swab.

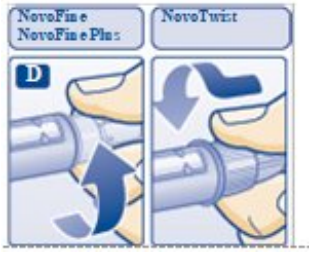
Before you inject, there must be at least 12 units of insulin left in the cartridge to make sure the remaining insulin is evenly mixed. If there are less than 12 units left, use a new NovoLog Mix 70/30 FlexPen.

Attaching the needle

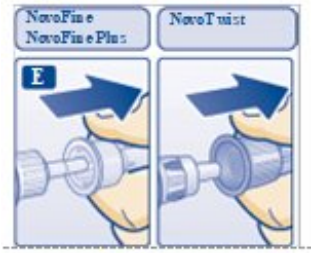
D. Remove the protective tab from a disposable needle.

Screw the needle tightly onto your NovoLog Mix 70/30 FlexPen. It is important that the needle is put on straight (see diagram D).

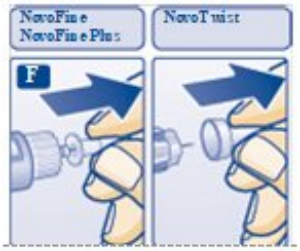
Never place a disposable needle on your NovoLog Mix 70/30 FlexPen until you are ready to take your injection.



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



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



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 or syringes with other people. You may give other people a serious infection, or get a serious infection from them.

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

To reduce the risk of a needle stick, **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 make sure you take the right dose of insulin**:

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



H. Hold your NovoLog Mix 70/30 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 H).



I. Keep the needle pointing upwards, press the push-button all the way in (see diagram I). 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 Mix 70/30 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.

J. 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 J). 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.



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 Mix 70/30 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.

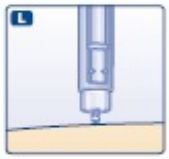
K. Insert the needle into your skin.

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

Turning the dose selector will not inject insulin.



L. 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 L). 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 Mix 70/30 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.

- 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, carefully slip the needle into the outer needle cap and throw it away in 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 Mix 70/30 FlexPen for your prescribed dose, the NovoLog Mix 70/30 FlexPen may be thrown away in your household trash after you have removed the needle. The NovoLog Mix 70/30 FlexPen prevents the cartridge from being completely emptied. It is designed to deliver 300 units.

M. Put the pen cap on the NovoLog Mix 70/30 FlexPen and store the NovoLog Mix 70/30 FlexPen without the needle attached (see diagram M). Storing without the needle attached helps prevent leaking, blocking of the needle, and air from entering the Pen.



How should I store NovoLog Mix 70/30 FlexPen?

- **Do not** freeze NovoLog Mix 70/30. **Do not** use NovoLog Mix 70/30 if it has been frozen.
- Keep NovoLog Mix 70/30 away from heat or light.
- Store the NovoLog Mix 70/30 FlexPen without the needle attached.
- **Unused NovoLog Mix 70/30 FlexPen:**
    - Store unused NovoLog Mix 70/30 FlexPen in the refrigerator at 36°F to 46°F (2°C to 8°C).
    - Unused NovoLog Mix 70/30 FlexPen may be used until the expiration date printed on the label, if kept in the refrigerator.
    - Unused NovoLog Mix 70/30 FlexPen should be thrown away after 14 days, if it is stored at room temperature.
- **In-Use NovoLog Mix 70/30 FlexPen:**
    - Store the FlexPen you are currently using at room temperature below 86°F (30°C) for up to 14 days.
    - The NovoLog Mix 70/30 FlexPen you are using should be thrown away after 14 days, even if it still has insulin left in it.

Maintenance

For the safe and proper use of your NovoLog Mix 70/30 FlexPen be sure to handle it with care. Avoid dropping your NovoLog Mix 70/30 FlexPen as it may damage it. If you are concerned that your NovoLog Mix 70/30 FlexPen is damaged, use a new one. You can clean the outside of your NovoLog Mix 70/30 FlexPen by wiping it with a damp cloth. Do not soak or wash your NovoLog Mix 70/30 FlexPen as it may damage it. Do not refill your NovoLog Mix 70/30 FlexPen.

⚠ Remove the needle from the NovoLog Mix 70/30 FlexPen after each injection. This

helps to ensure sterility, prevent leakage of insulin, and will help to make sure you inject the right dose of insulin for future injections.

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

 Keep your NovoLog Mix 70/30 FlexPen and needles out of the reach of children.

 Use NovoLog Mix 70/30 FlexPen as directed to treat your diabetes.

 **Do not** share your NovoLog Mix 70/30 FlexPen or needles with other people. You may give other people a serious infection, or get a serious infection from them.

 Always use a new needle for each injection.

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

 As a precautionary measure, always carry a spare insulin delivery device in case your NovoLog Mix 70/30 FlexPen is lost or damaged.

 Remember to keep the disposable NovoLog Mix 70/30 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.

Manufactured by:

Novo Nordisk Inc.

800 Scudders Mill Road

Plainsboro, New Jersey 08536

1-800-727-6500

U.S. License Number 1261

Revised: 2/2023

PRINCIPAL DISPLAY PANEL - VIAL 10ML

NDC 0169-3685-12

List 368512

NovoLog® Mix 70/30

(insulin aspart protamine and

insulin aspart) injectable suspension

100 units/mL (U-100)

For subcutaneous use.

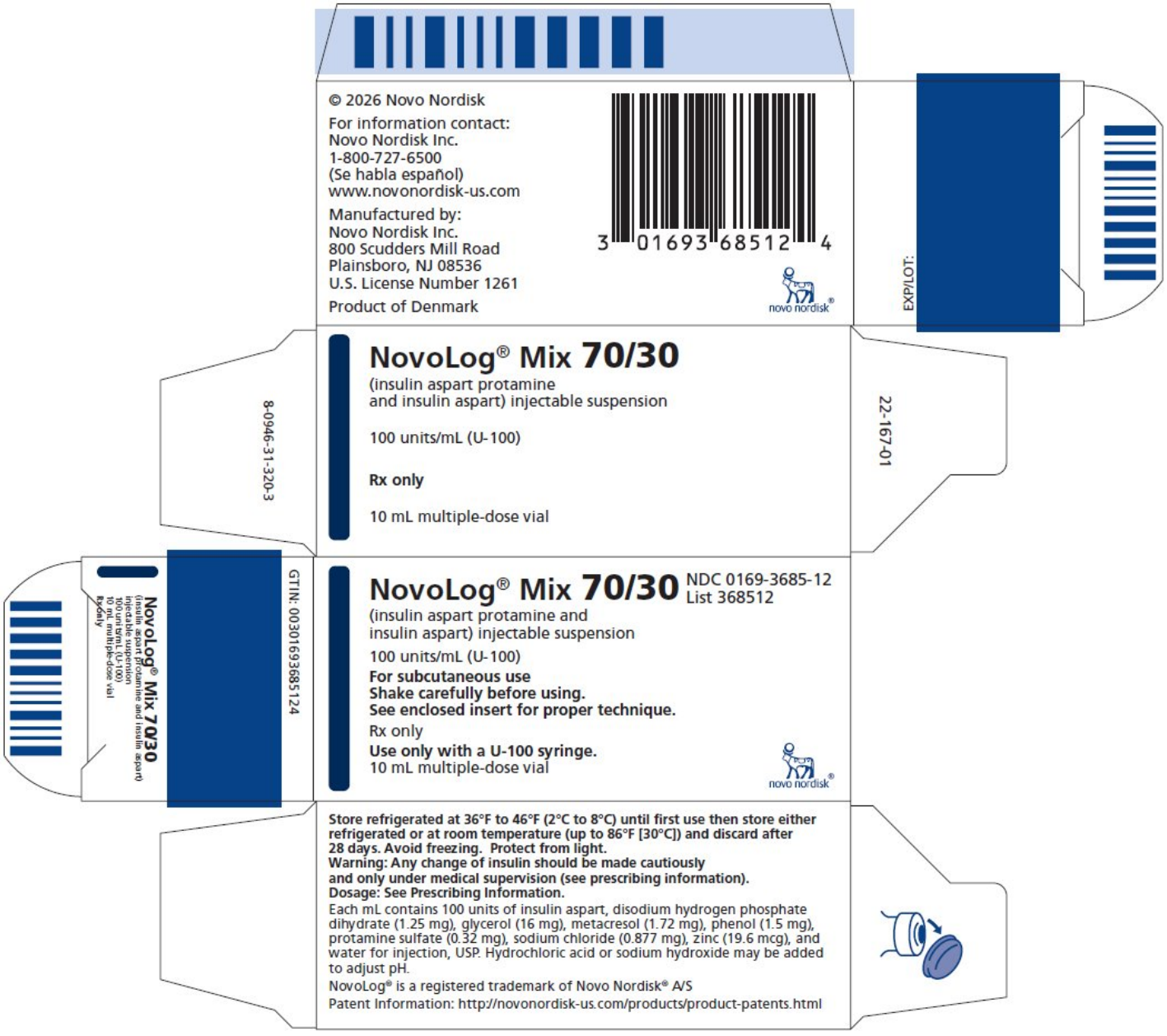
Shake carefully before using.

See enclosed insert for proper technique.

Rx only

Use only with a U-100 syringe.

10 mL multiple-dose vial



Principal Display Panel – Vial ReliOn®

NDC 0169-2200-11

List 220011

NovoLog® Mix 70/30

(insulin aspart protamine

and insulin aspart) injectable suspension

100 units/mL (U-100)

For subcutaneous use.

Shake carefully before using.

See enclosed insert for proper technique.

Rx only

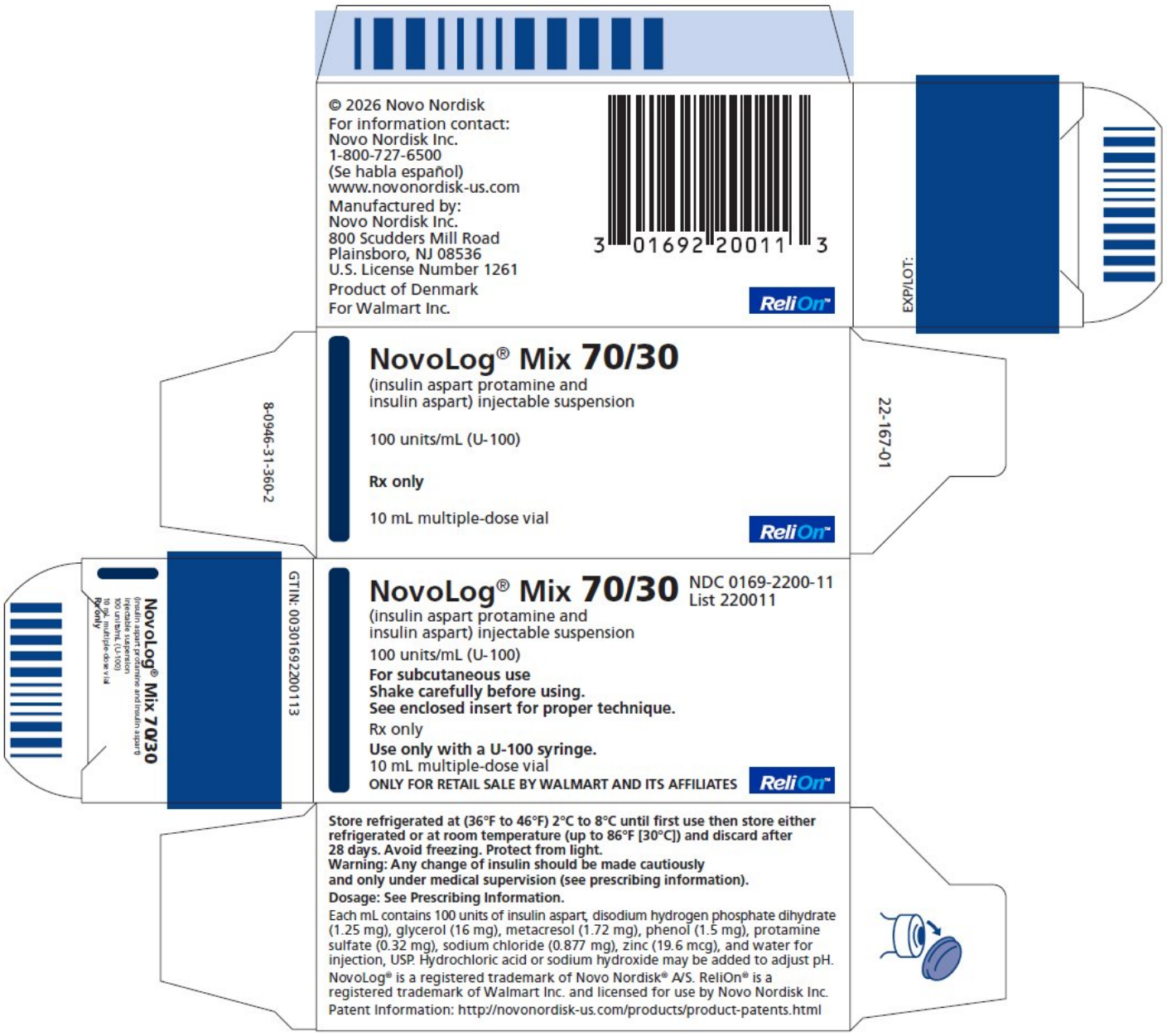
Use only with a U-100 syringe.

10 mL multiple-dose vial

ONLY FOR RETAIL SALE BY WALMART

AND ITS AFFILIATES

ReliOn®



PRINCIPAL DISPLAY PANEL - FLEXPEN 3ML

NDC 0169-3696-19

List 369619

NovoLog® Mix 70/30

FlexPen® Prefilled Pen

(insulin aspart protamine and

insulin aspart) injectable suspension

For Single Patient Use Only

100 units/mL (U-100)

5×3 mL prefilled pens

For subcutaneous use.

Shake carefully before using.

See enclosed insert for proper technique.

For use with NovoFine®, NovoFine® Plus or NovoTwist® disposable needles.

Store refrigerated at 2°C to 8°C (36°F to 46°F) until first use. After first use store at room temperature (up to 30°C [86°F]) and discard after 14 days. Avoid freezing. Protect from light.

Rx only

Dispense in this sealed carton.



Principal Display Panel FlexPen ReliOn®

NDC 0169-2201-25

List 220125

NovoLog® Mix 70/30

FlexPen® Prefilled Pen

(insulin aspart protamine and

insulin aspart) injectable suspension

For Single Patient Use Only

100 units/mL (U-100)

5×3 mL prefilled pens

For subcutaneous use.

Shake carefully before using.

See enclosed insert for proper technique.

For use with NovoFine®, NovoFine® Plus or NovoTwist® disposable needles.

Store refrigerated at 2°C to 8°C (36°F to 46°F) until first use.

After first use store at room temperature (up to 30°C [86°F]) and discard after 14 days. Avoid freezing. Protect from light.

Rx only

Dispense in this sealed carton.

ONLY FOR RETAIL SALE BY WALMART AND ITS AFFILIATES

ReliOn®



NOVOLOG MIX 70/30

insulin aspart injection, suspension

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0169-3685
Route of Administration	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
HYDROCHLORIC ACID (UNII: QTT17582CB)	
GLYCERIN (UNII: PDC6A3C0OX)	16.0 mg in 1 mL
METACRESOL (UNII: GGO4Y809LO)	1.72 mg in 1 mL
PHENOL (UNII: 339NCG44TV)	1.5 mg in 1 mL
PROTAMINE SULFATE (UNII: 0DE9724IHC)	0.32 mg in 1 mL
SODIUM CHLORIDE (UNII: 451W47IQ8X)	0.877 mg in 1 mL
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
ZINC (UNII: J41CSQ7QDS)	19.6 ug in 1 mL
WATER (UNII: 059QF0KO0R)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:0169-3685-12	1 in 1 CARTON	11/01/2001	
1		10 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		
2	NDC:0169-3685-92	1 in 1 CARTON	11/01/2001	02/28/2021
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	BLA021172	11/01/2001	

NOVOLOG MIX 70/30

insulin aspart injection, suspension

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0169-3696
Route of Administration	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
PROTAMINE SULFATE (UNII: 0DE9724IHC)	0.32 mg in 1 mL
SODIUM CHLORIDE (UNII: 451W47IQ8X)	0.877 mg in 1 mL
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
ZINC (UNII: J41CSQ7QDS)	19.6 ug in 1 mL
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0169-3696-19	5 in 1 CARTON	09/11/2002	
1		3 mL in 1 SYRINGE; Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)		
2	NDC:0169-3696-97	1 in 1 CARTON	09/11/2002	10/31/2016
2		3 mL in 1 SYRINGE; Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)		
3	NDC:0169-3696-98	1 in 1 CARTON	09/11/2002	11/30/2020
3	NDC:0169-3696-90	3 mL in 1 SYRINGE; 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	BLA021172	09/11/2002	

NOVOLOG MIX 70/30

insulin aspart injection, suspension

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0169-2200
Route of Administration	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
HYDROCHLORIC ACID (UNII: QTT17582CB)	
GLYCERIN (UNII: PDC6A3C0OX)	16.0 mg in 1 mL
METACRESOL (UNII: GGO4Y809LO)	1.72 mg in 1 mL
PHENOL (UNII: 339NCG44TV)	1.5 mg in 1 mL
PROTAMINE SULFATE (UNII: 0DE9724IHC)	0.32 mg in 1 mL
SODIUM CHLORIDE (UNII: 451W47IQ8X)	0.877 mg in 1 mL
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
ZINC (UNII: J41CSQ7QDS)	19.6 ug in 1 mL
WATER (UNII: 059QF0KO0R)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:0169-2200-11	1 in 1 CARTON	07/01/2021	
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	BLA021172	11/01/2001	

NOVOLOG MIX 70/30

insulin aspart injection, suspension

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0169-2201
Route of Administration	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
PROTAMINE SULFATE (UNII: 0DE9724IHC)	0.32 mg in 1 mL
SODIUM CHLORIDE (UNII: 451W47IQ8X)	0.877 mg in 1 mL
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
ZINC (UNII: J41CSQ7QDS)	19.6 ug in 1 mL
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0169-2201-25	5 in 1 CARTON	07/01/2021	
1		3 mL in 1 SYRINGE; 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	BLA021172	09/11/2002	

Labeler - Novo Nordisk Pharmaceutical Industries, LP (622920320)

Revised: 2/2023 Novo Nordisk Pharmaceutical Industries, LP