Getting Started on NovoLog® Mix 70/30 FlexPen®

A discreet, prefilled, dial-a-dose insulin pen

- Works with Novo Nordisk pen needles
- Prefilled with 300 units of insulin
- Large, clear dosing window
- Accurate and adjustable dose setting in 1-unit increments
- Push-button injection

**NovoLog® Mix 70/30 FlexPen® use**
- Never share with anyone, even if you attach a new pen needle
- Use a new pen needle for every injection
- Remove pen needle after every injection and discard into a puncture-resistant container
- Never place a disposable pen needle on NovoLog® Mix 70/30 FlexPen® until you’re ready to use it
- If NovoLog® Mix 70/30 FlexPen® isn’t working properly, perform a function check according to the Patient Instructions for Use on back

**NovoLog® Mix 70/30 FlexPen®** is about the size of a fountain pen and fits neatly inside a pocket or purse.

And it lasts up to 14 days without refrigeration after first use, so it can be taken almost anywhere.

**Detailed guidance is a call, click, or visit away**

**Novo Nordisk Customer Care**
Call 1-800-727-6500 to speak with a customer care representative about NovoLog® Mix 70/30

**Physician & Pharmacist**
Contact your doctor or pharmacist to learn more about NovoLog® Mix 70/30

**Cornerstones4Care®**
Support and diabetes management tools built around you. Enroll today to get FREE, personalized diabetes support at Cornerstones4Care.com

**Indications and Usage**

What is NovoLog® Mix 70/30 (70% insulin aspart protamine suspension and 30% insulin aspart injection, [rDNA origin])?
- NovoLog® Mix 70/30 is a man-made insulin used to control high blood sugar in adults with diabetes mellitus.
- It is not known if NovoLog® Mix 70/30 is safe or effective in children.

**Important Safety Information**

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.

Who should not use NovoLog® Mix 70/30?
- Do not use NovoLog® Mix 70/30 if your blood sugar is too low (hypoglycemia) or you are allergic to any of its ingredients.

Please see additional Important Safety Information on next page. Please see accompanying Prescribing Information.
A Guide to Using Your NovoLog® Mix 70/30 FlexPen®

Prepare your pen:

- Remove the cap
  Let the insulin reach room temperature before you use it. This makes it easier to mix. Then remove the cap.
- Mixing your insulin
  Roll the pen between your palms 10 times — keep the pen horizontal. Then gently move the pen up and down 10 times so the glass ball moves from one end of the cartridge to the other.
- Attach a new needle
  Remove the protective tab from a disposable needle and twist the needle on until it is tight. Pull off both needle caps.
- Prime your pen
  To remove any air in the cartridge, turn the dose selector to select 2 units. Press and hold the dose button. Make sure a drop appears.

Give your injection:

- Select your dose
  Turn the dose selector to select the number of units you need to inject.
- Give your injection
  Insert the needle. Press and hold the dose button. After the dose counter reaches 0, slowly count to 6.\(^1\)
- After the injection
  Carefully remove the needle and place it in a sharps container. Put the pen cap back on the NovoLog® Mix 70/30 FlexPen®.

Important Safety Information (cont'd)

What should I tell my health care provider before taking NovoLog® Mix 70/30?
- About all of your medical conditions, including liver, kidney, or heart problems.
- If you are pregnant, breastfeeding, or plan to do either.
- About all prescription and nonprescription medicines you take, including supplements, as your dose may need to change.

How should I take NovoLog® Mix 70/30?
- NovoLog® Mix 70/30 starts acting fast. If you have type 1 diabetes, inject within 15 minutes before you eat a meal. If you have type 2 diabetes, inject within 15 minutes before or after starting your meal.
- Inject NovoLog® Mix 70/30 under the skin of your stomach area, upper arms, buttocks, or thighs, but never into a vein or muscle.
- Do not mix NovoLog® Mix 70/30 with other insulin products or use in an insulin pump.
- Do not change your dose or type of insulin unless you are told to by your health care provider.
- 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.
- Check your blood sugar levels as directed by your health care provider.

What should I consider while using NovoLog® Mix 70/30?
- Alcohol, including beer and wine, may affect your blood sugar.
- Be careful when driving a car or operating machinery. You may have difficulty concentrating or reacting if you have low blood sugar. Talk to your health care provider if you often have low blood sugar or no warning signs of low blood sugar.

What are the possible side effects of NovoLog® Mix 70/30?
- Low blood sugar, including when too much is taken. Some symptoms include sweating, shakiness, confusion, and headache. Severe low blood sugar can cause unconsciousness, seizures, and death.
- Serious allergic reactions may occur. Get medical help right away, if you develop a rash over your whole body, have trouble breathing, a fast heartbeat, or sweating.
- Other side effects include low potassium in your blood, injection site reactions (like redness, swelling, and itching), skin thickening or pits at the injection site, weight gain, swelling of your hands and feet, if taken with thiazolidinediones (TZDs) possible heart failure, and vision changes.

Always 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.

Please note that if the needle is removed before the 6-second count is completed after the dose counter returns to “0,” then underdosing may occur by as much as 20%, resulting in the need for increasing the frequency of checking blood sugar and possible additional insulin administration.

Please see additional Important Safety Information on previous page.
Please see accompanying Prescribing Information.
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 (70% insulin aspart protamine suspension and 30% insulin aspart injection, (rDNA origin))

Suspension for subcutaneous injection

Initial U.S. Approval: 2001

— DOSAGE AND ADMINISTRATION —

• Only for subcutaneous injection (2.1).
  Type 1 DM: dose within 15 minutes before meal initiation.
  Type 2 DM: dose within 15 minutes before or after starting a meal.
• Do not administer intravenously (2.1).
• Do not use in insulin infusion pumps (2.1).
• Must be resuspended immediately before use (2.2).

— 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).
• NovoLog® Mix 70/30 should not be mixed with any other insulin product (5).
• Hypoglycemia is the most common adverse effect of insulin therapy. Glucose monitoring is recommended for all patients with diabetes. Any change of insulin dose should be made cautiously and only under medical supervision (5.2, 5.3).
• Insulin, particularly when given in settings of poor glycemic control, can cause hypokalemia. Use caution in patients predisposed to hypokalemia (5.4).
• Like all insulins, NovoLog® Mix 70/30 requirements may be reduced in patients with renal impairment or hepatic impairment (5.5, 5.6).
• Severe, life-threatening, generalized allergy, including anaphylaxis, may occur with insulin products, including NovoLog® Mix 70/30 (5.7).
• Fluid retention and heart failure can occur with concomitant use of thiazolidinediones (TZDs), which are PPAR-gamma agonists, and insulin, including NovoLog® Mix 70/30 (5.9).

ADVERSE REACTIONS

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

DRUG INTERACTIONS

• The following may increase the blood-glucose-lowering effect and susceptibility to hypoglycemia: oral antidiabetic products, pramlintide; ACE inhibitors, diisopyramide, fibrates, fluoxetine, monoamine oxidase (MAO) inhibitors, propoxyphene, salicylates, somatostatin analog (e.g. octreotide), sulfonamide antibiotics (7).
• The following may reduce the blood-glucose-lowering effect: corticosteroids, niacin, danazol, diuretics, sympathomimetic agents (e.g. epinephrine, salbutamol, terbutaline), lisoniazid, phenothiazine derivatives, somatropin, thyroid hormones, estrogens, progestogens (e.g., in oral contraceptives), atypical antipsychotics (7).
• Beta-blockers, clonidine, lithium salts, and alcohol may either potentiate or weaken the blood-glucose-lowering effect of insulin (7).
• Pentamidine may cause hypoglycemia, which may be followed by hyperglycemia (7).
• The signs of hypoglycemia may be reduced or absent in patients taking sympatholytic products such as beta-blockers, clonidine, guanethidine, and reserpine (7).

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

Revised: 02/2015
FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE
NovoLog® Mix 70/30 is an insulin analog indicated to improve glycemic control in patients with diabetes mellitus.

2 DOSAGE AND ADMINISTRATION
2.1 Dosing
NovoLog® Mix 70/30 is an insulin analog with an earlier onset and intermediate duration of action in comparison to the basal human insulin premix. The addition of protamine to the rapid-acting aspart insulin analog (NovoLog®) results in insulin activity that is 30% short-acting and 70% long-acting. NovoLog® Mix 70/30 is typically dosed on a twice-daily basis (with each dose intended to cover 2 meals or a meal and a snack). The dosage of NovoLog® Mix 70/30 must be individualized. The written prescription for NovoLog® Mix 70/30 should include the full name, to avoid confusion with NovoLog® (insulin aspart) and Novolin® 70/30 (human premix).

NovoLog® Mix 70/30 should appear uniformly white and cloudy. Do not use it if it looks clear or if it contains solid particles. NovoLog® Mix 70/30 should not be used after the printed expiration date.

NovoLog® Mix 70/30 should be administered by subcutaneous injection in the abdominal region, buttocks, thigh, or upper arm. NovoLog® Mix 70/30 has a faster onset of action than human insulin premix 70/30 and should be dosed within 15 minutes before meal initiation for patients with type 1 diabetes. For patients with type 2 diabetes, dosing should occur within 15 minutes before or after meal initiation. Injection sites should be rotated within the same region to reduce the risk of lipodystrophy. As with all insulins, the duration of action may vary according to the dose, injection site, blood flow, temperature, and level of physical activity.

NovoLog® Mix 70/30 should not be administered intravenously or used in insulin infusion pumps. Dose regimens of NovoLog® Mix 70/30 will vary among patients and should be determined by the health care professional familiar with the patient's metabolic needs, metabolic needs, eating habits, and other lifestyle variables.

2.2 Resuspension
NovoLog® Mix 70/30 is a suspension that must be visually inspected and resuspended immediately before use.

The NovoLog® Mix 70/30 vial should be rolled gently in your hands in a horizontal position 10 times to mix it. The rolling procedure must be repeated until the suspension appears uniformly white and cloudy. Inject immediately. Resuspension is easier when the insulin has reached room temperature.

The NovoLog® Mix 70/30 FlexPen® should be rolled 10 times gently between your hands in a horizontal position. Thereafter, turn the NovoLog® Mix 70/30 FlexPen® upside down so that the ball glass moves from one end of the reservoir to the other. Do this at least 10 times. The rolling and turning procedure must be repeated until the suspension appears uniformly white and cloudy. Inject immediately. Before each subsequent injection, turn the disposable NovoLog® Mix 70/30 FlexPen® upside down so that the ball glass moves from one end of the reservoir to the other at least 10 times and until the suspension appears uniformly white and cloudy. Inject immediately.

3 DOSAGE FORMS AND STRENGTHS
NovoLog® Mix 70/30 is available in the following package sizes: each presentation contains 100 units of insulin aspart per mL (U-100).

- 10 mL vials
- 3 mL NovoLog® Mix 70/30 FlexPen®

4 CONTRAINDICATIONS
NovoLog® Mix 70/30 is contraindicated
- during episodes of hypoglycemia
- in patients with hypersensitivity to NovoLog® Mix 70/30 or one of its excipients.

5 WARNINGS AND PRECAUTIONS
5.1 Never Share a NovoLog® Mix 70/30 FlexPen® Between Patients
NovoLog® Mix 70/30 FlexPen®s must never be shared between patients, even if the needle is changed. Pen-sharing poses a risk for transmission of blood-borne pathogens.

5.2 Administration
The short and long-acting components of insulin mixes, including NovoLog® Mix 70/30, cannot be titrated independently. Because NovoLog® Mix 70/30 has peak pharmacodynamic activity between 1-4 hours after injection, it should be administered within 15 minutes of meal initiation [see Clinical Pharmacology (12)]. The dose of insulin required to provide adequate glycemic control for one of the meals may result in hyper- or hypoglycemia for the other meal. The pharmacodynamic profile may also be inadequate for patients who require more frequent meals.

NovoLog® Mix 70/30 should not be mixed with any other insulin product.

NovoLog® Mix 70/30 should not be used intravenously.

NovoLog® Mix 70/30 should not be used in insulin infusion pumps.

Glucose monitoring is recommended for all patients with diabetes. This may present a risk in situations where these abilities are especially important for the patient, such as driving or operating machinery. Rapid changes in serum glucose levels may induce symptoms of hypoglycemia in persons with diabetes, regardless of the glucose value. Early warning symptoms of hypoglycemia may be different or less pronounced under certain conditions, such as long duration of diabetes, diabetic nerve disease, use of medications such as beta-blockers, or intensified diabetes control [see Drug Interactions (7)].

The timing of hypoglycemia may reflect the time-action profile of the insulin formulation [see Clinical Pharmacology (12)]. Other factors, such as changes in dietary intake (e.g., amount of food or timing of meals), injection site, exercise, and concomitant medications may also alter the risk of hypoglycemia [see Drug Interactions (7)]. As with all insulins, use caution in patients with hypoglycemia unawareness and in patients who may be predisposed to hypoglycemia (e.g., patients who are fasting or have erratic food intake). The patient’s ability to concentrate and react may be impaired as a result of hypoglycemia. This may present a risk in situations where these abilities are especially important, such as driving or operating machinery.

5.4 Hypokalemia
All insulin products, including NovoLog® Mix 70/30, cause a shift in potassium from the extracellular to intracellular space, possibly leading to hypokalemia that, if left untreated, may cause respiratory paralysis, ventricular arrhythmia, and death. Use caution in patients who may be at risk for hypokalemia (e.g. patients using potassium-lowering medications or patients taking medications sensitive to potassium concentrations).

5.5 Renal Impairment
Clinical or pharmacology studies with NovoLog® Mix 70/30 in diabetic patients with various degrees of renal impairment have not been conducted. As with other insulins, the requirements for NovoLog® Mix 70/30 may be reduced in patients with renal impairment [see Clinical Pharmacology (12.3)].

5.6 Hepatic Impairment
Clinical or pharmacology studies with NovoLog® Mix 70/30 in diabetic patients with various degrees of hepatic impairment have not been conducted. As with other insulins, the requirements for NovoLog® Mix 70/30 may be reduced in patients with hepatic impairment [see Clinical Pharmacology (12.3)].

5.7 Hypersensitivity and Allergic Reactions
Local Reactions - As with other insulin therapy, patients may experience 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 cases, may require discontinuation of NovoLog® Mix 70/30. In some instances, these reactions may be related to the insulin molecule, other components in the insulin preparation including protamine and cresol, components in skin cleansing agents, or injection techniques. Localized reactions and generalized myalgias have been reported with the use of cresol as an injectable excipient.

Systemic Reactions - Less common, but potentially more serious, is generalized allergy to insulin, which may cause rash (including pruritus) over the whole body, shortness of breath, wheezing, reduction in blood pressure, rapid pulse, or sweating. Severe cases of generalized allergy, including anaphylactic reaction, may be life threatening.

5.8 Antibody Production
Specific anti-insulin antibodies as well as cross-reacting anti-insulin antibodies were monitored in a 3-month, open-label comparator trial as well as in a long-term extension trial. Changes in cross-reactive antibodies were more common after NovoLog® Mix 70/30 than with conventional insulin. However, these changes did not correlate with change in HbA1c or increase in insulin dose. In this study, antibodies did not increase further after long-term exposure (>6 months) to NovoLog® Mix 70/30. The presence of such insulin antibodies may necessitate adjustment of the insulin dose in order to correct a tendency towards hyperglycemia or hypoglycemia.

5.9 Fluid retention and heart failure can occur 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
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.

- Hypoglycemia
Hypoglycemia is the most commonly observed adverse reaction in patients using insulin, including NovoLog® Mix 70/30 [see Warnings and Precautions (5.2)]. NovoLog® Mix 70/30 should not be used during episodes of hypoglycemia [see Contraindications (4) and Warnings and Precautions (5)].

- Insulin injection 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 lipoatrophy (thinning of adipose tissue) and lip hypertrophy (thickening of adipose tissue), and may affect insulin absorption. Rotate insulin injection sites within the same region to reduce the risk of lipodystrophy.

- Weight gain
Weight gain can occur with some insulin therapies, including NovoLog® Mix 70/30, and has been attributed to the anabolic effects of insulin and the decrease in glycosuria.

- Peripheral Edema
Insulin may cause sodium retention and edema, particularly in previously poor metabolic control is improved by intensified insulin therapy.

- Frequencies of adverse drug reactions
The frequencies of adverse drug reactions during a clinical trial with NovoLog® Mix 70/30 in patients with type 1 diabetes mellitus and type 2 diabetes mellitus are listed in the tables below. 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.
NovoLog® Mix 70/30 (70% insulin aspart protamine suspension and 30% insulin aspart injection, [rDNA origin])

Table 1: Treatment-Emergent Adverse Events in Patients with Type 1 diabetes mellitus (Adverse events with frequency ≥ 5% are included.)

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>NovoLog® Mix 70/30 (N=55)</th>
<th>NovoLog® 70/30 (N=49)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoglycemia</td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Headache</td>
<td>38</td>
<td>69</td>
</tr>
<tr>
<td>Influenza-like symptoms</td>
<td>7</td>
<td>13</td>
</tr>
<tr>
<td>Dypnea</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>Back pain</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Diaphoresis</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Rhinitis</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Skeletal pain</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>3</td>
<td>5</td>
</tr>
</tbody>
</table>

Table 2: Treatment-Emergent Adverse Events in Patients with Type 2 diabetes mellitus (Adverse events with frequency ≥ 5% are included.)

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>NovoLog® Mix 70/30 (N=85)</th>
<th>NovoLog® 70/30 (N=102)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoglycemia</td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Headache</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>Diaphoresis</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Rhinitis</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

Postmarketing Data
Additional 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. They include medication errors in which other insulins have been accidentally substituted for NovoLog® Mix 70/30 (see Patient Counseling Information (17)).

7 DRUG INTERACTIONS
A number of substances affect glucose metabolism and may require insulin dose adjustment and particularly close monitoring.

- The following are examples of substances that may increase the blood-glucose-lowering effect and susceptibility to hypoglycemia: oral antidiabetic products, pramlintide, ACE inhibitors, disopramide, fibrates, fluoxetine, monoamine oxidase (MAO) inhibitors, propranolol, salicylates, somatostatin analog (e.g. octreotide), sulfamethoxazole.
- The following are examples of substances that may reduce the blood-glucose-lowering effect: corticosteroids, niacin, dexamethasone, diuretics, sympathomimetic agents (e.g., ephedrine, salbutamol, terbutaline), isoniazid, phenothiazine derivatives, somatostatin analog, thyroid hormones, estrogens, progestogens (e.g., in oral contraceptives), atypical antipsychotics.
- Beta-blockers, clonidine, lithium salts, and alcohol may either potentiate or weaken the blood-glucose-lowering effect of insulin.
- Pentamidine may cause hypoglycemia, which may sometimes be followed by hyperglycemia.
- The signs of hypoglycemia may be reduced or absent in patients taking sympatholytic products such as beta-blockers, clonidine, guanethidine, and reserpine.

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Pregnancy Category B.

All pregnancies have a background risk of birth defects, loss, or other adverse outcome regardless of drug exposure. This background risk is increased in pregnancies complicated by hyperglycemia and may be decreased with good metabolic control. It is essential for patients with diabetes or history of gestational diabetes to maintain good metabolic control before conception and throughout pregnancy. Insulin requirements may decrease during the first trimester, generally increase during the second and third trimesters, and rapidly decline after delivery. Careful monitoring of glucose control is essential in such patients.

An open-label, randomized study compared the safety and efficacy of NovoLog® (the rapid-acting component of NovoLog® Mix 70/30) versus human insulin in the treatment of pregnant women with type 1 diabetes (222 exposed pregnancies (NovoLog®: 157, human insulin: 165)). Two-thirds of the enrolled patients were already pregnant when they entered the study. Since only one-third of the patients enrolled before conception, the study was not large enough to evaluate the risk of congenital malformations. Mean HbA1c of ~6% was observed in both groups during pregnancy, and there was no significant difference in the incidence of maternal hypoglycemia.

Animal reproduction studies have not been conducted with NovoLog® Mix 70/30. However, subcutaneous reproduction and teratology studies have been performed with NovoLog® (the rapid-acting component of NovoLog® Mix 70/30) and regular human insulin in rats and rabbits. In these studies, NovoLog® was given to female rats before mating, during mating, and throughout pregnancy, and to rabbits during organogenesis. The effects of NovoLog® did not differ from those observed with subcutaneous regular human insulin. NovoLog®, like human insulin, caused pre- and post-implantation losses and visceral/skeletal abnormalities in rats at a dose of 200 U/kg/day (approximately 32-times the human subcutaneous dose of 1.0 U/kg/day, based on U/body surface area), and in rabbits at a dose of 10 U/kg/day (approximately three times the human subcutaneous dose of 1.0 U/kg/day, based on U/body surface area). The effects are probably secondary to maternal hypoglycemia at high doses. No significant effects were observed in rats at a dose of 50 U/kg/day and rabbits at a dose of 3 U/kg/day. These doses are approximately 8 times the human subcutaneous dose of 1.0 U/kg/day for rats and equal to the human subcutaneous dose of 1.0 U/kg/day for rabbits based on U/body surface area.

Female patients should be advised to discuss with their physician if they intend to, or if they become pregnant. There are no adequate and well-controlled studies of the use of NovoLog® Mix 70/30 in pregnant women.

8.2 Nursing Mothers
It is unknown whether insulin aspart is excreted in human milk as occurs with human insulin. There are no adequate and well-controlled studies of the use of NovoLog® Mix 70/30 or NovoLog® in lactating women.

8.3 Pediatric Use
Safety and effectiveness of NovoLog® Mix 70/30 have not been established in pediatric patients.

8.4 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 patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dose range and titrating upward.

10 OVERDOSAGE
Hypoglycemia may occur as a result of an excess of insulin relative to food intake, energy expenditure, or both. 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.

12.3 Pharmacokinetics
The single substitution of the amino acid proline with aspartic acid at position 28 in insulin aspart (NovoLog®) reduces the molecule’s tendency to form hexamers as observed with regular human insulin.

Bioavailability and Absorption - The relative bioavailability of NovoLog® Mix 70/30 compared to NovoLog® and Novolin® 70/30 indicates that the insulins are absorbed to similar extent. In euglycemic clamp studies of healthy volunteers (n=23) after dosing with NovoLog® Mix 70/30 (0.2 U/kg), a mean maximum serum concentration (Cmax) of 23.4 ± 5.3 mU/L was reached after 60 minutes. The mean half-life (t1/2) of NovoLog® Mix 70/30 was about 8 to 9 hours. Serum insulin levels returned to baseline 15 to 18 hours after a subcutaneous dose of NovoLog® Mix 70/30. Similar data were seen in a separate euglycemic clamp study in healthy volunteers (n=24) after dosing with NovoLog®...
Mix 70/30 (0.3 U/kg). A C_max of 61.3 ± 20.1 mIU/L was reached after 85 minutes. Serum insulin levels returned to baseline 12 hours after a subcutaneous dose.

The C_max and the area under the insulin concentration-time curve (AUC) after administration of NovoLog® Mix 70/30 was approximately 20% greater than those after administration of Novolin® 70/30, (see Fig. 3 for pharmacokinetic profiles).

Distribution and Elimination - NovoLog® has a low binding to plasma proteins, 0 to 9%, similar to regular human insulin. After subcutaneous administration in normal male volunteers (n=24), NovoLog® was more rapidly eliminated than regular human insulin with an average apparent half-life of 81 minutes compared to 141 minutes for regular human insulin.

The effect of sex, age, obesity, ethnic origin, renal and hepatic impairment, pregnancy, or smoking, on the pharmacodynamics and pharmacokinetics of NovoLog® Mix 70/30 has not been studied.

### 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 U/kg/day (approximately 2, 8, and 32 times the human subcutaneous dose of 1.0 U/kg/day, based on U/body surface area, respectively). At a dose of 200 U/kg/day, NovoLog® increased the incidence of mammary gland tumors in females when compared to untreated controls. The incidence of mammary tumors found with NovoLog® was not significantly different from that found with regular human insulin. 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 vitro 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 U/kg/day (approximately 32 times the human subcutaneous dose, based on U/body surface area) had no direct adverse effects on male and female fertility, or on general reproductive performance of animals.

#### 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. However, the effect of NovoLog® Mix 70/30 is more rapid in onset compared to Novolin® (human insulin) 70/30 due to its faster absorption after subcutaneous injection.

### 14 CLINICAL STUDIES

#### 14.1 NovoLog® Mix 70/30 versus Novolin® 70/30

In a three-month, open-label trial, patients with type 1 (n=104) or type 2 (n=187) diabetes 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 HbA1C were comparable across the treatment groups (see Table 3).

<table>
<thead>
<tr>
<th>Treatment 24-weeks</th>
<th>HbA1C Baseline ± SD (n)</th>
<th>NovoLog® Mix 70/30 + Metformin + Pioglitazone</th>
<th>Metformin + Pioglitazone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjusted Mean change from baseline ± SD (n)*</td>
<td>-1.6 ± 0.1 (93)</td>
<td>-0.3 ± 0.1 (87)</td>
<td>-1.3 ± 0.1 (-1.6, -1.0)</td>
</tr>
<tr>
<td>Percentage of subjects reaching HbA1C &lt;7.0%</td>
<td>76%</td>
<td>24%</td>
<td>74%</td>
</tr>
<tr>
<td>Percentage of subjects reaching HbA1C ≤5.5%</td>
<td>59%</td>
<td>12%</td>
<td>59%</td>
</tr>
</tbody>
</table>

#### 14.2 Combination Therapy: Insulin and Oral Agents in Patients with Type 2 Diabetes

**Trial 1:**

In a 34-week, open-label trial, insulin-naive patients with type 2 diabetes currently treated with 2 oral antidiabetic agents were switched to treatment with metformin and pioglitazone. During an 8-week optimization period metformin and pioglitazone were increased to 2500 mg per day and 50 or 45 mg per day, respectively. After the optimization period, subjects 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 IU twice daily (before breakfast and before supper). Insulin doses were titrated to a pre-meal glucose goal of 80-110 mg/dL. The metformin dose was adjusted to 2500 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 Caucasian (53%), and the mean initial weight was 90 kg.

**Trial 2:**

In a 28-week, open-label trial, insulin-naive patients with type 2 diabetes with fasting plasma glucose above 140 mg/dL currently treated with metformin plus a 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 5). NovoLog® Mix 70/30 was started at an average dose of 5-6 IU (0.07 ± 0.03 IU/kg) twice daily (before breakfast and before supper), and bedtime insulin glargine was started at 10-12 IU (0.13 ± 0.03 IU/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 2500 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 Caucasian (53%), and the mean initial weight was 90 kg.

### REFERENCES


### 16 HOW SUPPLIED/STORAGE AND HANDLING

#### 16.1 How Supplied

NovoLog® Mix 70/30 is available in the following package sizes: each presentation contains 100 Units of insulin aspart per mL (U-100).

- 10 mL vials (NDC 0169-3956-15)
- 3 mL NovoLog® Mix 70/30 FlexPen® (NDC 0169-3969-19)

NovoLog® Mix 70/30 vials and NovoLog® Mix 70/30 FlexPen® are latex free. NovoLog® Mix 70/30 FlexPen®s must never be shared between patients, even if the needle is changed.

#### 16.2 Recommended Storage

Unused NovoLog® Mix 70/30 should be stored in a refrigerator between 2°C and 8°C (36°F to 46°F). Do not store in the freezer or refrigeration.
directly adjacent to the refrigerator cooling element. Do not freeze NovoLog® Mix 70/30 or use NovoLog® Mix 70/30 if it has been frozen.

**Vials:** After initial use, a vial may be kept at temperatures below 30°C (86°F) for up to 28 days, but should not be exposed to excessive heat or sunlight. Open vials may be refrigerated.

Unpunctured vials can be used until the expiration date printed on the label if they are stored in a refrigerator. Keep unused vials in the carton so they will stay clean and protected from light.

NovoLog® Mix 70/30 FlexPen®: Once a NovoLog® Mix 70/30 FlexPen® is punctured, it should be kept at temperatures below 30°C (86°F) for up to 14 days, but should not be exposed to excessive heat or sunlight. A NovoLog® Mix 70/30 FlexPen® in use must NOT be stored in the refrigerator. Keep the disposable NovoLog® Mix 70/30 FlexPen® away from direct heat and sunlight. An unpunctured NovoLog® Mix 70/30 FlexPen® can be used until the expiration date printed on the label if they are stored in a refrigerator. Keep any unused NovoLog® Mix 70/30 FlexPen® in the carton so it will stay clean and protected from light.

Always remove the needle after each injection and store NovoLog® Mix 70/30 FlexPen® without a needle attached. This prevents contamination and/or infection, or leakage of insulin, and will ensure accurate dosing. Always use a new needle for each injection to prevent contamination.

These storage conditions are summarized in the following table:

<table>
<thead>
<tr>
<th>NovoLog® Mix 70/30 FlexPen®</th>
<th>Not in-use (unopened) Room Temperature (below 30°C [86°F])</th>
<th>Not in-use (unopened) Refrigerated Temperature (2°C - 8°C [36°F - 46°F])</th>
<th>In-use (opened) Room Temperature (below 30°C [86°F])</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 mL vial</td>
<td>28 days</td>
<td>Until expiration date</td>
<td>28 days (refrigerated/room temperature)</td>
</tr>
<tr>
<td>3 mL NovoLog® Mix 70/30</td>
<td>14 days</td>
<td>Until expiration date</td>
<td>14 days (Do not refrigerate)</td>
</tr>
</tbody>
</table>

17 **PATIENT COUNSELING INFORMATION**

[see FDA-Approved Patient Labeling]

17.1 **Never Share a NovoLog® Mix 70/30 FlexPen® Between Patients**

Advise patients that they must never share a NovoLog® Mix 70/30 FlexPen® with another person, even if the needle is changed, because doing so carries a risk for transmission of bloodborne pathogens.

17.2 **Physician Instructions**

Maintenance of normal or near-normal glucose control is a treatment goal in diabetes mellitus and has been associated with a reduction in diabetic complications. Patients should be informed about potential risks and advantages of NovoLog® Mix 70/30 therapy including the possible adverse reactions. Patients should also be offered continued education and advice on insulin therapies, injection technique, life-style management, regular glucose monitoring, periodic glycosylated hemoglobin testing, recognition and management of hypo- and hyperglycemia, adherence to meal planning, complications of insulin therapy, timing of dose, instruction for use of injection devices, and proper storage of insulin. See Patient Information supplied with the product. Patients should be informed that frequent, patient-performed blood glucose measurements are needed to achieve optimal glycosylated control and avoid both hyper- and hypoglycemia, and diabetic ketoacidosis.

The patient’s ability to concentrate and react may be impaired as a result of hypoglycemia. This may present a risk in situations where these abilities are especially important, such as driving or operating other machinery. Patients who have frequent hypoglycemia or reduced or absent warning signs of hypoglycemia should be advised to use caution when driving or operating machinery.

Accidental substitutions between NovoLog® Mix 70/30 and other insulin products have been reported. Patients should be instructed to always carefully check that they are administering the appropriate insulin to avoid medication errors between NovoLog® Mix 70/30 and any other insulin. **The prescription for NovoLog® Mix 70/30 should be written clearly in order to avoid confusion with other insulin products, for example, NovoLog® or Novolin® 70/30. In addition, the written prescription should clearly indicate the presentation, for example FlexPen® or vial.**
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.

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

Your insulin dose may need to change because of:
- change in level of physical activity or exercise
- weight gain or loss
- increased stress
- illness
- change in diet

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.

What are the ingredients in NovoLog® Mix 70/30?
Active Ingredient: 70% insulin aspart protamine suspension and 30% insulin aspart (rDNA origin).
Inactive Ingredients: glycerol, phenol, metacresol, zinc, disodium hydrogen phosphate dihydrate, sodium chloride, protamine sulfate, water for injection, hydrochloric acid or sodium hydroxide.
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: 04/2015
Instructions for Use
NovoLog® Mix 70/30 (Nø-vø-Log-MIX-SEV-en-tee-TIR-tee) (70% insulin aspart protamine suspension and 30% insulin aspart [rDNA origin] injection)
10 mL 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 swab

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 one 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).
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.
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).
Step 5: Push the needle through the rubber stopper of the NovoLog® Mix 70/30 vial (See Figure E).
Step 6: Push the plunger all the way in. This puts air into the NovoLog® Mix 70/30 vial (See 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).
Step 8: Slowly push the plunger up until the black tip reaches the line for your NovoLog® Mix 70/30 dose (See 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).
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).
Step 12: Insert the needle into your skin. Push down on the plunger to inject your dose (See Figure L). Needle should remain in the skin for at least 6 seconds to make sure you have injected all the insulin.
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.

After your injection:
- Do not recap the needle. Recapping the needle can lead to a needle stick injury.
- Throw away empty insulin vials, used syringes and needles in a sharps container or some type of hard plastic or metal container with a screw on cap such as a detergent bottle or coffee can. Check with your healthcare provider about the right way to throw away the container. There may be local or state laws about how to throw away used syringes and needles. Do not throw away used syringes and needles in household trash or recycling bins.

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.
- Store opened and unopened NovoLog® Mix 70/30 vials in the refrigerator at 36°F to 46°F (2°C to 8°C). Opened NovoLog® Mix 70/30 vials can also be stored out of the refrigerator below 86°F (30°C).
- Unopened vials may be used until the expiration date printed on the label, if they are kept in the refrigerator.
- Opened NovoLog® Mix 70/30 vials should be thrown away 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.

Revised: March 2013
NovoLog® is a registered trademark of Novo Nordisk A/S. NovoLog® Mix 70/30 is covered by US Patent No. 5,866,538 and other patents pending.
Manufactured by: Novo Nordisk A/S
DK-2880 Bagsvaerd, Denmark
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
© 2002-2015 Novo Nordisk 0415-00206644-1 5/2015
Instructions For Use

NovoLog® Mix 70/30 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 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.

NovoLog® Mix 70/30 FlexPen® should not be used by people who are blind or have severe visual problems without the help of a person who has good eyesight and who is trained to use the NovoLog® Mix 70/30 FlexPen® the right way.

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 be 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.

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 dispose of it (see diagram F).

Always use a new needle for each injection to help ensure sterility and 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.

∆ 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) or your stomach area, buttocks, upper legs (thighs), or upper arms.
• For each injection, change (rotate) your injection site within the area of skin that you use. Do not use the same injection site for more than 24 units selected

K. Insert the needle into your skin.
   Inject the dose by pressing the push-button all the way in until the O 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. 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 NovoLog® Mix 70/30 FlexPen® and needles in a FDA-cleared sharps disposal container right away after use. Do not throw away (dispose of) loose needles and Pens in your household trash.
• If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
  - made of a heavy-duty plastic
  - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out
  - upright and stable during use
  - leak-resistant
  - properly labeled to warn of hazardous waste inside the container

• When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. 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.

The NovoLog® Mix 70/30 FlexPen® prevents the cartridge from being completely emptied. It is designed to deliver 300 units.

How should I store 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).
• Store the FlexPen® you are currently using out of the refrigerator below 86°F (30°C) for up to 14 days.
• 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.
• Unused NovoLog® Mix 70/30 FlexPen® may be used until the expiration date printed on the label, if kept in the refrigerator.
• 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.
• Store the NovoLog® Mix 70/30 FlexPen® without the needle attached.

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.

Revised: 04/2015