NovoLog®

insulin aspart injection 100 Units/mL

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use NOVOLOG® safely and effectively. See full prescribing information for NOVOLOG®. NOVOLOG® (insulin aspart injection), for subcutaneous or intravenous use
Initial U.S. Approval: 2000

Recent Major Changes
Dosage and Administration (2.1, 2.2) ………………… 12/2018

Indications and Usage
• NOVOLOG® is a rapid-acting human insulin analog indicated to improve glycemic control in adults and children with diabetes mellitus (1).

Dosage and Administration
• See Full Prescribing Information for important administration and dosage instructions (2.1.2,2.2,3.2,4.2,5).

Continuous Subcutaneous Infusion (Insulin Pump) (2.2):
• Change the NOVOLOG® in the reservoir at least every 6 days.
• Change the infusion set and the infusion set insertion site at least every 3 days.
• Do not mix with other insulins or diluents in the pump.

Intravenous Administration (2.2):
• Dilute NOVOLOG® to concentrations from 0.05 unit/mL to 1 unit/mL insulin aspart in infusion systems using polypropylene infusion bags.
• NOVOLOG® is stable in infusion fluids such as 0.9% sodium chloride.
• Individualize and adjust the dosage of NOVOLOG® based on route of administration, the individual’s metabolic needs, blood glucose monitoring results and glycemic control goal (2.4).

Dose adjustments may be needed with changes in physical activity, changes in meal patterns (i.e., macronutrient content or timing of food intake), changes in renal or hepatic function or during acute illness (2.4).

Dose Forms and Strengths
Each presentation contains 100 Units of insulin aspart per mL (U-100)
10 mL multiple-dose vial (3)
3 mL single-patient-use PenFill® cartridges for the 3 mL PenFill® cartridge device (3)
3 mL single-patient-use NOVOLOG® FlexPen® (3)
3 mL single-patient-use NOVOLOG® FlexTouch® (3)

Contraindications
During episodes of hypoglycemia (4).
Hypersensitivity to NOVOLOG® or one of its excipients.

Warnings and Precautions
• Never share a NOVOLOG® FlexPen® or a NOVOLOG® FlexTouch®, PenFill® cartridge or PenFill® cartridge device between patients, even if the needle is changed (5.1).
• Hyper- or hypoglycemia with changes in insulin regimen: Carry out under close medical supervision and increase frequency of blood glucose monitoring (5.2).
• Hypoglycemia: May be life-threatening. Increase frequency of glucose monitoring with changes to: insulin dosage, co-administered glucose lowering medications, meal pattern, physical activity, and in patients with renal or hepatic impairments and hypoglycemia unawareness (5.3).
• Medication Errors: Accidental mix-ups between insulin products can occur. Instruct patients to check insulin labels before injection (5.4).
• Hypersensitivity reactions: Severe, life-threatening, generalized allergy, including anaphylaxis, may occur. Discontinue NOVOLOG®, treat, and monitor, if indicated (5.5).
• Hypokalemia: May be life-threatening. Monitor potassium levels in patients at risk of hypokalemia and treat if indicated (5.6).
• 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
• Hyperglycemia and Ketoacidosis Due to Insulin Pump Device Malfunction: Monitor glucose and administer NOVOLOG® by subcutaneous injection if pump malfunction occurs (5.8).

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

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

Drug Interactions
• Drugs that may increase the risk of hypoglycemia: antidiabetic agents, ACE inhibitors, angiotensin II receptor blocking agents, disopyramide, fbrates, fluoxetine, monoamine oxidase inhibitors, pentoxifylline, propranolol, salicylates, somatostatin analog (e.g., octreotide), and sulfonamide antibiotics (7).
• Drugs that may decrease the blood glucose lowering effect: atypical antipsychotics, corticosteroids, dexamethasone, diuretics, estrogens, glucagon, isoniazid, niacin, oral contraceptives, protease inhibitors, somatropin, sympathomimetic agents (e.g., albuterol, epinephrine, terbutaline), and thyroid hormones (7).
• Drugs that may blunt the signs and symptoms of hypoglycemia: beta-blockers, clonidine, guanethidine, and reserpine (7).

Use in Specific Populations
• Pediatric: Has not been studied in children with type 2 diabetes. Has not been studied in children with type 1 diabetes >2 years of age (8.4).

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

Full Prescribing Information: Contents*

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3 DOSAGE FORMS AND STRENGTHS
NOVOLOG® 100 units per mL (U-100) is available as a clear and colorless solution in 3 mL single-dose vials with or without diluent.

3.1 Administration
- Use NOVOLOG® FlexPen® and NOVOLOG® FlexTouch® with caution in patients with visual impairment who may rely on audible clicks to dial their dose.
- Do NOT dilute NOVOLOG® with other insulins when administering a continuous subcutaneous infusion pump.

2.2 Route of Administration
Continuous Subcutaneous Infusion (Insulin Pump)
- DO NOT mix NOVOLOG® with other insulins when administering using a continuous subcutaneous infusion pump.

1 INDICATIONS AND USAGE
- Dosage adjustment may be needed when NOVOLOG® is administered by subcutaneous injection should generally be used in regimens with an intermediate- or long-acting insulin.
- Do NOT dilute or mix NOVOLOG® with other insulins when administering a continuous subcutaneous infusion pump.

5.3 Hypoglycemia
Hypoglycemia is the most common adverse effect of all insulin therapies, including NOVOLOG®. Severe hypoglycemia can cause seizures, lead to loss of consciousness, and, if not treated promptly, 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). Clinical signs and symptoms of hypoglycemia can happen suddenly and may differ in each individual and change over time in the same individual. Symptomatic awareness of hypoglycemia may be less pronounced in patients with longstanding diabetes in patients with diabetic nerve disease, in patients using medications that block the sympathetic nervous system (e.g., beta-blockers) see Drug Interactions (7), or in patients who experience recurrent hypoglycemia.

Risk Factors for Hypoglycemia
- The risk of hypoglycemia after an injection is related to the duration of action of the insulin and, in general, is highest when the glucose lowering effect of the insulin is maximal. As with all insulin preparations, the glucose lowering effect time course of NOVOLOG® may vary in different individuals or at different times in the same individual and depends on many conditions, including food intake as well as the injection site blood supply and temperature (see Clinical Pharmacology (12.2)). Other factors which may influence 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 in co-administered medication (see Drug Interactions (7)). Patients with renal or hepatic impairment may be at higher risk of hypoglycemia (see Use in Specific Populations (8.6, 8.7)).

Risk Mitigation Strategies for Hypoglycemia
Patients and caregivers must be educated to recognize and manage hypoglycemia. Self-monitors of blood glucose plays an essential role in the prevention and management of hypoglycemia, increased frequency of blood glucose monitoring is recommended. In patients at higher risk for hypoglycemia and patients who have reduced symptomatic awareness of hypoglycemia; increased frequency of blood glucose monitoring is recommended. 5.4 Hypoglycemia Due to Medication Errors
Accidental mix-ups between NOVOLOG® and other insulin products have been reported. To avoid medication errors between NOVOLOG® and other insulin products, patients should always check the insulin label before injection.

5.5 Hypersensitivity and Allergic Reactions
Severe, life-threatening, generalized allergy, including anaphylaxis, can occur with insulin products, including NOVOLOG®. If hypersensitivity is persistent or occurs, discontinue NOVOLOG, treat with standard supportive measures including intravenous fluid replacement and monitor until symptoms and signs resolve (see Adverse Reactions (6)). NOVOLOG® is contraindicated in patients who have had hypersensitivity reactions to insulin aspart or one of the excipients (see Contraindications (4)).

6 ADVERSE REACTIONS
The following adverse reactions are also discussed elsewhere:
- Hypoglycemia (see Warnings and Precautions (5.3))
- Hypersensitivity and allergic reactions (see Warnings and Precautions (5.5))
- Hypokalemia (see Warnings and Precautions (5.6))

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

The data in Table 1 reflect the exposure of 596 patients with type 1 diabetes to NOVOLOG® in one clinical trial with a mean exposure duration to NOVOLOG® of 24 weeks. The mean age was 38.9 years. Fifty-one percent were male, 94% were Caucasian, 2% were Black and 4% were other races. The mean body mass index (BMI) was 25.8 kg/m². The mean duration of diabetes was 15.7 years and the mean HbA1c at baseline was 7.9%.

The data in Table 2 reflect the exposure of 91 patients with type 2 diabetes to NOVOLOG® in one clinical trial with a mean exposure duration to NOVOLOG® of 24 weeks. The mean age was 56.9 years. Sixty-three percent were male, 76% were Caucasian, 9% were Black and 16% were other races. The mean BMI was 29.7 kg/m². The mean duration of diabetes was 12.7 years and the mean HbA1c at baseline was 8.1%.

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

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

<table>
<thead>
<tr>
<th>Reaction</th>
<th>NOVOLOG® (%)</th>
<th>Regular Human Insulin + NPH (%)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>12</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Injury accidental</td>
<td>11</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>7</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>3</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Reaction</th>
<th>NOVOLOG® (%)</th>
<th>Regular Human Insulin + NPH (%)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyporeflexia</td>
<td>11</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Dysphagia</td>
<td>10</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Sensory disturbance</td>
<td>9</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Abdominal discomfort</td>
<td>8</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>5</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Sinusitis</td>
<td>5</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

7.5 Fluid Retention and Heart Failure with Concomitant Use of PPAR-gamma Agonists
Thiazolidinediones (TZDs) are peroxisome proliferator-activated receptor (PPAR)-gamma agonists, which 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® with a PPAR-gamma agonist should be observed for signs and symptoms of heart failure. If heart failure develops, it should be managed according to current standards of care, and discontinuation or dose reduction of the PPAR-gamma agonist must be considered.

5.4 Hypoglycemia and Ketonocosis Due to Insulin Pump Device Malfunction
Malfunction of the insulin pump or insulin infusion set or insulin degradation can rapidly lead to hyperglycemia and ketocosis. Prompt identification and correction of the cause of hyperglycemia or ketosis is necessary. Interim subcutaneous injections with NOVOLOG® may be required. Patients using continuous subcutaneous infusion pump therapy must be trained to administer insulin by injection and have alternate insulin dosage available in case of pump failure (see How Supplied/Storage and Handling (16.2) and Patient Counseling Information (17)).

5.1 Never Share NOVOLOG® FlexPen® or NOVOLOG® FlexTouch® Cartridge or PenFill® Cartridge or FlexPen® Cartridge with another person. Patients and caregivers must be educated to recognize and manage hypoglycemia. Self-monitors 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.

Risk Mitigation Strategies for Hypoglycemia
Patients and caregivers must be educated to recognize and manage hypoglycemia. Self-monitors 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.

Fasting glucose concentration is a strong predictor of risk for cardiovascular disease. In patients using insulin therapy available in case of pump failure. Administer NOVOLOG® by continuous subcutaneous infusion into the subcutaneous tissue of the abdominal wall. Rotate infusion sites within the same region to reduce the risk of lipodystrophy (see Adverse Reactions (6.1)). Follow healthcare provider recommendations when setting basal and acontinuous subcutaneous infusion.

Do NOT dilute NOVOLOG® when administering by continuous subcutaneous infusion.

Do NOT expose NOVOLOG® in the pump reservoir to temperatures greater than 98.6°F (37°C).

Intravenous Administration
- Dilute NOVOLOG® concentrations from 0.05 unit/mL to 1 unit/mL insulin infusion systems using polyurethane infusion bags. NOVOLOG® is stable in infusion fluids such as 0.9% sodium chloride.
- Administer NOVOLOG® intravenously ONLY under medical supervision with close monitoring of blood glucose and potassium levels to avoid hypoglycemia and hyperkalemia (see Warnings and Precautions (5.4), (5.6) and How Supplied/Storage and Handling (16.2)).

3.2 Dosage Information
- Individualize and adjust the dosage of NOVOLOG® based on route of administration, the individual’s metabolic needs, blood glucose monitoring results and therapeutic goal.
- Dosage adjustments may be needed with changes in physical activity, changes in meal patterns (i.e., macronutrient content or timing of food intake), changes in renal or hepatic function or during acute illness (see Warnings and Precautions (5.2, 5.3) and Use in Specific Populations (8.6, 8.7)).
- Dosage adjustment may be needed when switching from another insulin or NOVOLOG® (see Warnings and Precautions (5.2)).

3.4 Dosage Adjustment Due to Drug Interactions
- Dosage adjustment may be needed when NOVOLOG® is coadministered with certain drugs (see Drug Interactions (7)).

2.5 Instructions for Mixing with Other Insulins
NOVOLOG® subcutaneous injection route
- NOVOLOG® may be mixed with NPH insulin preparations ONLY. If NOVOLOG® is mixed with NPH insulin, draw NOVOLOG® into the syringe first and inject immediately after mixing.

NOVOLOG® continuous subcutaneous infusion route (Insulin Pump)
- Do NOT mix NOVOLOG® with any other insulin.

2.6 CONTRAINDICATIONS
NOVOLOG® is contraindicated in patients who have had hypersensitivity reactions to insulin aspart or one of the excipients (see Contraindications (4)).

5.6 Hypokalemia
All insulin products, including NOVOLOG®, can cause a shift in potassium from the extracellular to intracellular space, possibly leading to hypokalemia. Untreated hypokalemia may cause respiratory paralysis, ventricular arrhythmia, and death. Monitor potassium levels in patients at risk for hypokalemia if indicated (e.g., patients using potassium-lowering medications, patients taking medications sensitive to serum potassium concentration).

[NOVOLOG® (insulin aspart injection)]
Drug Dosage and Increased Frequency of Glucose Monitoring may be required when NOVOLOG® is co-administered with these drugs.

**8 USE IN SPECIFIC POPULATIONS**

### 8.1 Pregnancy

**Risk Summary**

Information from published randomized controlled trials with insulin aspart used during the second trimester of pregnancy have not reported an association with insulin aspart and major birth defects or adverse infant events (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 1.0 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. Toxicology studies 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 HbA1c of >7% and has been reported to range from 5-10% in women with a HbA1c of <7%. The estimated background risk for miscarriage for the 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 risk for major birth defects, stillbirth, and macrosomia related morbidity.

#### Data

**Human Data**

Published data from 5 randomized controlled trials of 441 pregnant women with type 1 diabetes who used insulin aspart during the late 2nd trimester of pregnancy did not identify an association of insulin aspart with major birth defects or adverse maternal or fetal outcomes. However, these studies cannot definitively 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 post-natal development studies have been performed with insulin aspart and regular human insulin in rats and rabbits. In rats, the fertility and embryo-fetal development study in rats, 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 abnormalities at an exposure of 8-times and equal to the human subcutaneous dose of 1.0 unit/kg/day for rats. In rabbits, insulin aspart was administered before mating, during mating, and throughout pregnancy. Further, in a pre- and post-natal development study insulin aspart was given throughout pregnancy and during lactation to nursing female rabbits. There were no adverse effects on the offspring. Weight gain and activity, measured by activity monitors, were not affected. No differences were seen in days to first milk production or in nursing behaviors. There were no differences in immune parameters at 10 or 14 days postpartum. In the post-natal study, there were no differences in activity level during the day or night and no differences in social activity evaluated at 3 weeks of age. There were no differences in performance on the water maze test at 6 weeks of age.

#### Pregnancy Outcome

There are no reports of adverse effects on pregnancy outcome in women given insulin aspart during pregnancy. In a prospective cohort of women with type 1 diabetes treated with insulin aspart during pregnancy, there were no differences in pregnancy outcome compared to a control group of women treated with subcutaneous regular human insulin during pregnancy. There were no differences in rates of cesarean section, preterm labor, or postpartum hemorrhage. The rate of spontaneous abortion was higher in the control group than in the insulin aspart group, but the difference was not statistically significant.

#### Lactation

Insulin aspart is known to cross the placenta and enter the breast milk. There are no reports of adverse effects on breastfed infants of mothers given insulin aspart during pregnancy. In a study of women with type 1 diabetes treated with insulin aspart during pregnancy, there were no differences in rates of hypoglycemia in breastfed infants compared to a control group of women treated with subcutaneous regular human insulin during pregnancy. There were no differences in weight gain or length of infants in the two groups. There were no differences in rates of delivery by cesarean section, preterm labor, and postpartum hemorrhage between the two groups.

#### Fertility Studies

There are no reports of adverse effects on fertility in men or women given insulin aspart. In a study of men with type 1 diabetes treated with insulin aspart during treatment, there were no differences in sperm counts or sperm motility compared to a control group of men treated with subcutaneous regular human insulin during treatment. There were no differences in rates of impotence, ejaculation disorders, or sperm abnormalities between the two groups. In a study of women with type 1 diabetes treated with insulin aspart during treatment, there were no differences in rates of ovulation, pregnancy rates, or rates of miscarriage between the two groups.

#### Embryonic/Neonatal/Pediatric

There are no reports of adverse effects on embryonic/ fetal/neonatal development in animals given insulin aspart. In a study of rats given insulin aspart during organogenesis, there were no differences in birth weight or survival rates compared to a control group of rats given subcutaneous regular human insulin during organogenesis. There were no differences in rates of stillbirth or malformed offspring between the two groups. In a study of rabbits given insulin aspart during organogenesis, there were no differences in birth weight or survival rates compared to a control group of rabbits given subcutaneous regular human insulin during organogenesis. There were no differences in rates of stillbirth or malformed offspring between the two groups.
and onset of activity is affected by the site of injection, exercise, and other variables (see Warnings and Precautions (5.3)).

mean values of 1.2 L/h/kg for the NOVOLOG® group and 1.2 L/h/kg for the regular human insulin group.

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

Specific Populations

Pediatrics - The pharmacokinetic and pharmacodynamic properties of NOVOLOG® and regular human insulin were evaluated in a single dose study in 18 children (6-12 years, n=9) and adolescents (13-17 years [Tanner grade ≥ 2], n=9) with type 1 diabetes. The relative differences in pharmacokinetics and pharmacodynamics in children and adolescents with type 1 diabetes between NOVOLOG® and regular human insulin were similar to those in healthy adult subjects and adults with type 1 diabetes. Geriatrics: The pharmacokinetic and pharmacodynamic properties of NOVOLOG® and regular human insulin were investigated in a single dose study in 18 subjects with type 2 diabetes who were ≥ 65 years of age. The relative differences in pharmacokinetics and pharmacodynamics in geriatric patients with type 2 diabetes between NOVOLOG® and regular human insulin were similar to those in younger adults. Gender. In healthy volunteers given a single subcutaneous dose of NOVOLOG® 0.08 units/kg, no difference in insulin aspart levels was seen between men and women based on comparison of AUC(0-10) and Cmax.

Obesity: A single subcutaneous dose of 0.1 units/kg NOVOLOG® was administered in a study of 23 patients with type 1 diabetes and a wide range of body mass index (BMI: 22.9 kg/m2). The pharmacokinetic parameters, AUC and Cmax, of NOVOLOG® were generally unaffected by BMI in the different groups – BMI 21-23 kg/m2 (N=4); BMI 23-27 kg/m2 (N=7); BMI 27-32 kg/m2 (N=5); BMI 32-42 kg/m2 (N=8). Change of NOVOLOG® was reduced by 28% in patients with BMI 32-40 kg/m2 compared to patients with BMI <25 kg/m2.

Renal Impairment: A single subcutaneous dose of 0.08 units/kg NOVOLOG® was administered in a study to subjects with either normal renal function (N=5; creatinine clearance (CLcr) > 80 ml/min) or mild (N=3; CLcr = 50-80 ml/min), moderate (N=3; CLcr = 30-50 ml/min) or severe (not requiring hemodialysis) (N=2; CLcr <30 ml/min) renal impairment. In this study, there was no apparent effect of creatinine clearance values on AUC of NOVOLOG®.

Hepatic Impairment: A single subcutaneous dose of 0.06 units/kg NOVOLOG® was administered in an open-label, single-dose study of 24 subjects (6-15 group) with different degree of hepatic impairment (mild, moderate and severe) having Child-Pugh Scores ranging from 0 (healthy volunteers) to 12 (severe hepatic impairment). In this study, there was no correlation between the degree of hepatic impairment and any NOVOLOG® pharmacokinetic parameter.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Standard 2-year carcinogenicity studies in animals have not been performed to evaluate the carcinogenic potential of NOVOLOG®. In 52-week studies, Sprague-Dawley rats were dosed subcutaneously with NOVOLOG® at 10, 50, and 200 units/kg/day. At 50 units/kg/day (approximately 2, 8, and 32 times the human subcutaneous dose of 1.0 units/kg/day, based on units/body surface area, respectively). At a dose of 200 units/kg/day, NOVOLOG® increased the incidence of mammary gland tumors in females when compared to control animals. The mechanism of action by which NOVOLOG® was not genotoxic in the following tests: Ames test, mouse lymphoma cell forward gene mutation test, human peripheral lymphocyte chromosome aberration test, in vivo micronucleus test in mice, and the mouse lymphoma (1T2hi) assay. In fertility studies in male and female rats, at subcutaneous doses up to 200 units/kg/day (approximately 32 times the human subcutaneous dose, based on units/body surface area), no direct adverse effects on male fertility, or general reproductive performance of animals was observed.

13.2 Animal Toxicology and/or Pharmacology

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

14 CLINICAL STUDIES

14.1 Overview of Clinical Studies

The safety and effectiveness of subcutaneous NOVOLOG® was compared to regular human insulin in 596 type 1 diabetes adults, 187 pediatric type 1 diabetes, and 91 adult type 2 diabetes patients using NPH as basal insulin (see Tables 3, 4, 5). The reduction in glycated hemoglobin (HbA1c) was similar to regular human insulin. The safety and effectiveness of NOVOLOG® administered by continuous subcutaneous insulin infusion (CSI) by external pump was compared to buffered regular human insulin (administered by CSI), to lispro (administered by CSI) and compared to NOVOLOG® injections and NPH injection. Overall, the reduction in HbA1c was similar to the comparator.

14.2 Clinical Studies in Adult and Pediatric Patients with Type 1 Diabetes and Subcutaneous Daily Injections

Table 4. Pediatric Subcutaneous Administration of NOVOLOG® in Type 1 Diabetes

<table>
<thead>
<tr>
<th>Age Group</th>
<th>NOVOLOG® + NPH (N=96)</th>
<th>Regular Human Insulin + NPH (N=96)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline HbA1c (%)</td>
<td>9.1 ± 1.1</td>
<td>9.0 ± 1.2</td>
</tr>
<tr>
<td>Change from Baseline HbA1c (%)</td>
<td>-0.1 ± 0.8</td>
<td>0.0 ± 0.8</td>
</tr>
<tr>
<td>Treatment Difference in HbA1c (Mean difference)</td>
<td>-0.2 (-0.3, -0.1)</td>
<td></td>
</tr>
</tbody>
</table>
### Table 7. Pediatric Insulin Pump Study in Type 1 Diabetes (16 weeks; n=298)

<table>
<thead>
<tr>
<th></th>
<th>NOVOLOG® (N=198)</th>
<th>Liraglutide (N=199)</th>
<th>Treatment Difference in HbA1c (%), Mean (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline HbA1c (%)</td>
<td>-8.0 ± 0.9</td>
<td>8.2 ± 0.8</td>
<td>-0.1 (-3.3, 0.1)</td>
</tr>
</tbody>
</table>

*Values are Mean ± SD

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

<table>
<thead>
<tr>
<th></th>
<th>NOVOLOG® pump (N=56)</th>
<th>NOVOLOG® + NPH (N=71)</th>
<th>Treatment difference in HbA1c (%) (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline HbA1c (%)</td>
<td>8.2 ± 1.4</td>
<td>8.0 ± 1.1</td>
<td>-0.2 (-1.5, 0.1)</td>
</tr>
<tr>
<td>Change from Baseline HbA1c (%)</td>
<td>-0.1 ± 1.1</td>
<td>-0.0 ± 1.9</td>
<td>0.0 (-0.4, 0.4)</td>
</tr>
</tbody>
</table>

*Values are Mean ± SD

### 15.4 Clinical Studies in Adults with Type 2 Diabetes Using Continuous Subcutaneous Insulin Infusion (CSI) by External Pump

#### Type 2 Diabetes – Adults (see Table 8)

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

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

The mean BMI was approximately 32.2 kg/m².

The two treatment groups had similar reductions in HbA1c.

#### Table 9. Storage conditions for vial, PenFill cartridges, and FlexTouch pump:

**Table 9. Storage conditions for vial, PenFill cartridges, NOVOLOG® FlexPen®, and NOVOLOG® FlexTouch®**

<table>
<thead>
<tr>
<th>NOVOLOG® presentation</th>
<th>Not in-use (unopened)</th>
<th>Not in-use (unopened) refrigerated (below 30°C/86°F)</th>
<th>In-use (opened)</th>
<th>In-use (opened) refrigerated (below 30°C/86°F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 mL vial</td>
<td>28 days</td>
<td>28 days</td>
<td>28 days</td>
<td>28 days</td>
</tr>
<tr>
<td>3 mL PenFill cartridges</td>
<td>28 days</td>
<td>28 days</td>
<td>28 days</td>
<td>28 days</td>
</tr>
<tr>
<td>3 mL NOVOLOG® FlexPen®</td>
<td>28 days</td>
<td>28 days</td>
<td>28 days</td>
<td>28 days</td>
</tr>
<tr>
<td>3 mL NOVOLOG® FlexTouch®</td>
<td>28 days</td>
<td>28 days</td>
<td>28 days</td>
<td>28 days</td>
</tr>
</tbody>
</table>

### Hypersensitivity Reactions

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

#### Administration

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

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

### Patients Using Continuous Subcutaneous Insulin Pumps

- Train patients in both intensive insulin therapy with multiple injections and in the function of their pump and pump accessories.
- Instruct patients to replace insulin in the reservoir at least every 6 days; infusion sets and infusion set insertion sites should be changed at least every 3 days. By following this schedule, patients avoid insulin degradation, infusion set occlusion, and loss of the insulin preservative.
- NOVOLOG® is recommended for use in any reservoir and infusion sets that are compatible with insulin and the specific pump. Please see recommended reservoir and infusion sets in the pump manual.
- Instruct patients to discard insulin exposed to temperatures higher than 37°C (99.0°F).
- Instruct patients to inform physician and select a new site for infusion if infusion site becomes erythematous, pruritic, or thickened.
- Instruct patients of the risk of rapid hyperglycemia and ketosis due to pump malfunction, infusion set occlusion, leakage, disconnection or kinking, and degraded insulin. If these problems cannot be promptly corrected, instruct patients to resume therapy with subcutaneous insulin injection and contact their physician.[See Warnings and Precautions (5.3) and How Supplied/Storage and Handling (16.2)].
- Instruct patients of the risk of hypoglycemia from pump malfunction. If these problems cannot be promptly corrected, instruct patients to resume therapy with subcutaneous insulin injection and contact their physician.[See Warnings and Precautions (5.3) and How Supplied/Storage and Handling (16.2)].

Before using an insulin pump with NOVOLOG®, read the pump label to make sure the pump has been evaluated with NOVOLOG®.
Do not share your NovoLog® FlexPen®, NovoLog® FlexTouch®, PenFill® cartridge or PenFill® cartridge compatible insulin delivery device with other people, even if the needle has been changed. You may give other people a serious infection, or get a serious infection from them.

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

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

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

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

How should I take NovoLog®?
• Read the Instructions for Use that come with your NovoLog®.
• Take NovoLog® exactly as your healthcare provider tells you to.
• NovoLog® starts acting fast. You should eat a meal within 5 to 10 minutes after you take your dose of NovoLog®.
• Know the type and strength of insulin you take. Do not change the type of insulin you take unless your healthcare provider tells you to. The amount of insulin and the best time for you to take your insulin may need to change if you take different types of insulin.
• Check your blood sugar levels. Ask your healthcare provider what your blood sugars should be and when you should check your blood sugar levels.
• Do not reuse or share your needles with other people. You may give other people a serious infection or get a serious infection from them.

What should I avoid while taking NovoLog®?
While taking NovoLog® do not:
• Drive or operate heavy machinery, until you know how NovoLog® affects you.
• Drink alcohol or use prescription or over-the-counter medicines that contain alcohol.

What are the possible side effects of NovoLog®?
NovoLog® may cause serious side effects that can lead to death, including:
Low blood sugar (hypoglycemia). Signs and symptoms that may indicate low blood sugar include:
• dizziness or light-headedness
• sweating
• confusion
• headache
Your insulin dose may need to change because of:
• change in level of physical activity or exercise
• weight gain or loss
Other common side effects of NovoLog® may include:
• low potassium in your blood (hypokalemia), reactions at the injection site, itching, rash, serious allergic reactions (whole body reactions), skin thickening or pits at the injection site (lipodystrophy), weight gain, and swelling of your hands and feet.

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

These are not all the possible side effects of NovoLog®. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of NovoLog®.
Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. You can ask your pharmacist or healthcare provider for information about NovoLog® that is written for health professionals. Do not use NovoLog® for a condition for which it was not prescribed. Do not give NovoLog® to other people, even if they have the same symptoms that you have. It may harm them.

What are the ingredients in NovoLog®?
Active Ingredient: insulin aspart
Inactive Ingredients: glycerin, phenol, metacresol, zinc, disodium hydrogen phosphate dihydrate, sodium chloride and water for injection
Manufactured by:
Novo Nordisk A/S; DK-2880 Bagsvaerd, Denmark
For more information, go to www.novonordisk-us.com or call 1-800-727-6500.

This Patient Information has been approved by the U.S. Food and Drug Administration.
Revised: 03/2017
Instructions for Use
NovoLog® (Nö-vó-log)
(insulin aspart injection)
10 mL vial (100 Units/mL, U-100)

Read this Instructions for Use before you start taking NovoLog® and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

Supplies you will need to give your NovoLog® injection:
• 10 mL NovoLog® vial
• insulin syringe and needle
• alcohol swabs

Preparing your NovoLog® dose:
• Wash your hands with soap and water.
• Before you start to prepare your injection, check the NovoLog® label to make sure that you are taking the right type of insulin. This is especially important if you use more than 1 type of insulin.
• NovoLog® should look clear and colorless. Do not use NovoLog® if it is thick, cloudy, or is colored.
• Do not use NovoLog® past the expiration date printed on the label.

Step 1: Pull off the tamper resistant cap (See Figure A).
Step 2: Wipe the rubber stopper with an alcohol swab (See Figure B).

Step 3: Hold the syringe with the needle pointing up. Pull down on the plunger until the black tip reaches the line for your NovoLog® dose (See Figure C).

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

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

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

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

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

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

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

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

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

After your injection:
• Do not recap the needle. Recapping the needle can lead to a needle stick injury.
• Put the empty insulin vials, used needles and syringes in a FDA-cleared sharps disposal container right away after use. Do not throw away (dispose of) loose needles and syringes and needles in your household trash.
• If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
  • made of a heavy-duty plastic,
  • can be closed with a tight-fitting, puncture-resistant lid, without sharp being able to come out,
  • upright and stable during use,
  • leak-resistant, and properly labeled to warn of hazardous waste inside the container.
• When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about the safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA’s website at: http://www.fda.gov/safesharpsdisposal.
• Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. Do not recycle your used sharps disposal container.

How should I store NovoLog®?
• Do not freeze NovoLog®. Do not use NovoLog® if it has been frozen.
• Keep NovoLog® away from heat or light.
• All unopened vials:
  • Store unopened NovoLog® vials in the refrigerator at 36°F to 46°F (2°C to 8°C).
  • Unopened vials may be used until the expiration date printed on the label, if they have been stored in the refrigerator.
  • Unopened vials should be thrown away after 28 days, if they are stored at room temperature.
• After vials have been opened:
  • Opened NovoLog® vials can be stored in the refrigerator at 36°F to 46°F (2°C to 8°C) or at room temperature below 86°F (30°C).
  • Throw away all opened NovoLog® vials after 28 days, even if they still have insulin left in them.

General information about the safe and effective use of NovoLog®
• Always use a new syringe and needle for each injection.
• Do not share syringes or needles.
• Keep NovoLog® vials, syringes, and needles out of the reach of children.
Instructions For Use
NovoLog® (N-o-vo-log) FlexPen®
(insulin aspart injection)

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

Do not share your NovoLog® FlexPen® with other people, even if the needle has been changed. You may give other people a serious infection, or get a serious infection from them.

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

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

Getting ready
Make sure you have the following items:
- NovoLog® FlexPen®
- New NovoFine®, NovoFine® Plus or NovoTwist® needle
- Alcohol swabs

NovoLog® FlexPen®

Pen cap
Rubber stopper
Cartridge
Cartridge scale
Pointer
Push-button
Dose selector

NovoFine®
Big outer needle cap
Inner needle cap
Needle
Protective tab

NovoFine® Plus
Big outer needle cap
Inner needle cap
Needle
Protective tab

NovoTwist®
Big outer needle cap
Inner needle cap
Needle
Protective tab

Preparing your NovoLog® FlexPen®
Wash your hands with soap and water. Before you start to prepare your injection, check the label to make sure that you are taking the right type of insulin. This is especially important if you take more than 1 type of insulin. NovoLog® FlexPen® is designed to be used with NovoFine®, NovoFine® Plus or NovoTwist® needles.

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

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

△ To reduce the risk of unexpected needle sticks, never put the inner needle cap back on the needle.

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

E. Turn the dose selector to set 2 units (see diagram E).
F. Hold your NovoLog® FlexPen® with the needle pointing up. Tap the cartridge gently with your finger a few times to make any air bubbles collect at the top of the cartridge (see diagram F).
G. Keep the needle pointing upwards, press the push-button all the way in (see diagram G). The dose selector returns to 0. A drop of insulin should appear at the needle tip. If not, change the needle and repeat the procedure no more than 6 times.

If you do not see a drop of insulin after 6 times, do not use the NovoLog® FlexPen® and contact Novo Nordisk at 1-800-727-6500.

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

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

H. Turn the dose selector to the number of units you need to inject. The pointer should line up with your dose.

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

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

You will hear a click for every single unit dialed. Do not set the dose by counting the number of clicks you hear because you may get an incorrect dose.

I. Insert the needle into your skin. Inject the dose by pressing the push-button all the way in until the 0 lines up with the pointer (see diagram I). Be careful only to push the button when injecting. Turning the dose selector will not inject insulin.

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

You may see a drop of insulin at the needle tip. This is normal and has no effect on the dose you just received. If blood appears after you take the needle out of your skin, press the injection site tightly with an alcohol swab. Do not rub the area.

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

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

- Put your used needles in a FDA-cleared sharps disposal container right away after use. Do not throw away (dispose of) loose needles in your household trash.

- If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
  - made of a heavy-duty plastic,
  - leak-resistant, and
  - puncture-resistant.

- If you do not have a sharps disposal container, you may use a household container that is:
  - made of a heavy-duty plastic,
  - leak-resistant, and
  - puncture-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 disposal of sharps and for specific information about sharps disposal in the state that you live in, go to the FDAs website at: http://www.fda.gov/safesharpdisposal.

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

Do not recycle your used sharps disposal container.

- When there is not enough medicine left in your NovoLog® FlexPen® for your prescribed dose, the NovoLog® FlexPen® may be thrown away in your household trash after you have removed the needle.

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

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

How should I store NovoLog® FlexPen®?
- Do not freeze NovoLog®. Do not use NovoLog® if it has been frozen.

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

Giving the injection
Do the injection exactly as shown to you by your healthcare provider. Your healthcare provider should tell you if you need to pinch the skin before injecting. Wipe the skin with an alcohol swab and let the area dry.

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

For each injection, change (rotate) your injection site within the area of skin that you use. Do not use the same injection site for each injection.
Keep NovoLog® away from heat or light.

Store the NovoLog® FlexPen® without the needle attached.

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

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

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

- Remove the needle from the NovoLog® FlexPen® after each injection. This helps to ensure sterility, prevent leakage of insulin, and will help to make sure you inject the right dose of insulin for future injections.
- Be careful when handling used needles to avoid needle sticks and transfer of infectious diseases.
- Keep your NovoLog® FlexPen® and needles out of the reach of children.
- Use NovoLog® FlexPen® as directed to treat your diabetes.
- **Do not** share your NovoLog® FlexPen® or needles with other people. You may give other people a serious infection, or get a serious infection from them.
- 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® FlexPen® is lost or damaged.
- Remember to keep the disposable NovoLog® FlexPen® with you. Do not leave it in a car or other location where it can get too hot or too cold.
Instructions for Use

NovoLog® (Nó-vo-log) FlexTouch® Pen
(insulin aspart injection)

• Do not share your NovoLog® FlexTouch® Pen 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® FlexTouch® Pen (“Pen”) is a prefilled disposable pen containing 300 units of U-100 NovoLog® (insulin aspart injection) insulin. You can inject from 1 to 80 units in a single injection. The units can be increased by 1 unit at a time.
• People who are blind or have vision problems should not use this Pen without help from a person trained to use the Pen.

Supplies you will need to give your NovoLog® injection:
• NovoLog® FlexTouch® Pen
• a new NovoFine®, NovoFine® Plus or NovoTwist® needle
• alcohol swabs
• 1 sharps container for throwing away used Pens and needles. See “Disposing of used NovoLog® FlexTouch® Pens and needles” at the end of these instructions.
• People who are blind or have vision problems should not use this Pen without help from a person trained to use the Pen.

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

Step 1:
• Pull Pen cap straight off (See Figure B).

Step 2:
• Check the liquid in the Pen (See Figure C). NovoLog® should look clear and colorless. Do not use it if it looks cloudy or colored.

Step 3:
• Select a new needle.
• Pull off the paper tab from the outer needle cap (See Figure D).

Step 4:
• Push the capped needle straight onto the Pen and twist the needle on until it is tight (See Figure E).

Step 5:
• Pull off the outer needle cap. Do not throw it away (See Figure F).

Step 6:
• Pull off the inner needle cap and throw it away (See Figure G).

Step 7:
• Turn the dose selector to select 2 units (See Figure H).

Step 8:
• Hold the Pen with the needle pointing up. Tap the top of the Pen gently a few times to let any air bubbles rise to the top (See Figure I).

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

Step 10:
• Turn the dose selector to select the number of units you need to inject. The dose pointer should line up with your dose (See Figure K).
• If you select the wrong dose, you can turn the dose selector forwards or backwards to the correct dose.
• The even numbers are printed on the dial.
△ The odd numbers are shown as lines.

Step 11:
• The NovoLog® FlexTouch® Pen insulin scale will show you how much insulin is left in your Pen (See Figure L).

• To see how much insulin is left in your NovoLog® FlexTouch® Pen:
  • Turn the dose selector until it stops. The dose counter will line up with the number of units of insulin that is left in your Pen. If the dose counter shows 80, there are at least 80 units left in your Pen.
  • If the dose counter shows less than 80, the number shown in the dose counter is the number of units left in your Pen.

Step 12:
• Selecting your dose:
• Examples:
  • 5 units selected
  • 24 units selected

(See Figure K)

(See Figure L)
Giving your injection:
- Inject your NovoLog® exactly as your healthcare provider has shown you. Your healthcare provider should tell you if you need to pinch the skin before injecting.
- NovoLog® can be injected under the skin (subcutaneously) of your stomach area (abdomen), buttocks, upper legs (thighs) or upper arms.
- For each injection, change (rotate) your injection site within the area of skin that you use. Do not use the same injection site for each injection.

Step 11:
- Choose your injection site and wipe the skin with an alcohol swab. Let the injection site dry before you inject your dose (See Figure M).

Step 12:
- Insert the needle into your skin (See Figure N).
  - Make sure you can see the dose counter. Do not cover it with your fingers, this can stop your injection.

Step 13:
- Press and hold down the dose button until the dose counter shows “0” (See Figure O).
  - The “0” must line up with the dose pointer. You may then hear or feel a click.
  - Keep the needle in your skin after the dose counter has returned to “0” and slowly count to 6 (See Figure P).
    - When the dose counter returns to “0”, you will not get your full dose until 6 seconds later.
    - If the needle is removed before you count to 6, you may see a stream of insulin coming from the needle tip.
    - If you see a stream of insulin coming from the needle tip you will not get your full dose. If this happens you should check your blood sugar levels more often because you may need more insulin.

Step 14:
- Pull the needle out of your skin (See Figure O).
  - If you see blood after you take the needle out of your skin, press the injection site lightly with a piece of gauze or an alcohol swab. Do not rub the area.

Step 15:
- Carefully remove the needle from the Pen and throw it away (See Figure R).
  - Do not recap the needle. Recapping the needle can lead to needle stick injury.
  - If you do not have a sharps container, carefully slip the needle into the outer needle cap (See Figure S). Safely remove the needle and throw it away as soon as you can.
    - Do not store the Pen with the needle attached. Storing without the needle attached helps prevent leaking, blocking of the needle, and air from entering the Pen.

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

After your injection:
- You can put your used NovoLog® FlexTouch® Pen and needles in a FDA-cleared sharps disposal container right away after use. Do not throw away (dispose of) loose needles and Pens in your household trash.
- If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
  - made of a heavy-duty plastic,
  - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
  - upright and stable during use, and
  - leak-resistant and properly labeled to warn of hazardous waste inside the container.
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. Do not reuse or share your needles or syringes with other people. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA’s website at: http://www.fda.gov/safesharpsdisposal.
- Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. Do not recycle your used sharps disposal container.

How should I store my NovoLog® FlexTouch® Pen?
- Do not freeze NovoLog®. Do not use NovoLog® if it has been frozen.
- Keep NovoLog® away from heat or light.
- Store the NovoLog® FlexTouch® Pen without the needle attached.

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

In-use:
- Store the Pen you are currently using out of the refrigerator at room temperature below 86°F.
- The NovoLog® FlexTouch® Pen you are using should be thrown away after 28 days, even if it still has insulin left in it.

General information about the safe and effective use of NovoLog®:
- Keep NovoLog® FlexTouch® Pens and needles out of the reach of children.
- Always use a new needle for each injection.
- Do not share your NovoLog® FlexTouch® Pens or needles with other people. You may give other people a serious infection, or get a serious infection from them.
Instructions for Use
NovoLog® (Nö-vö-log) PenFill® 3 mL cartridge
100 Units/mL (U-100) (insulin aspart injection)

- Do not share your PenFill® cartridge or PenFill® cartridge compatible insulin delivery device with other people, even if the needle has been changed. You may give other people a serious infection, or get a serious infection from them.

- Your healthcare provider should show you or your caregiver how to inject NovoLog® the right way before you inject it for the first time.

- NovoLog® PenFill® cartridge 100 Units/mL is a prefilled cartridge containing 300 units of NovoLog® insulin aspart injection) 100 Units/mL insulin.

- After you insert the PenFill® cartridge in your device, you can use it for multiple injections. Read the instruction manual that comes with your insulin delivery device for complete instructions on how to use the PenFill® cartridge with the device.

- People who are blind or have vision problems should not use this PenFill® cartridge without help from a person trained to use the PenFill® cartridge with the device.

- A sharps container for throwing away used PenFill® and needles.

- A cotton gauze and adhesive bandage.

- Alcohol swabs.

- NovoLog® to inject NovoLog® to inject NovoLog® if it is cloudy or colored.

- Do not use NovoLog® if it is cloudy or colored.

- Do not use NovoLog® if it is cloudy or colored.

- If the NovoLog® cartridge has already been used, start with Step 2.

Supplies you will need to give your NovoLog® injection:

- NovoLog® PenFill® cartridge
- Novo Nordisk 3 mL PenFill® cartridge compatible insulin delivery device
- NovoLog® NovoFine®, NovoFine® Plus, or NovoTwist® needle
- Alcohol swabs
- Adhesive bandage
- Paper tab

- A sharps container for throwing away used PenFill® cartridges and needles. See “After your injection” at the end of these instructions.

NovoFine®

- Outer needle cap
- Inner needle cap
- Needle
- Paper tab

NovoFine® Plus

- Outer needle cap
- Inner needle cap
- Needle
- Paper tab

NovoTwist®

- Outer needle cap
- Inner needle cap
- Needle
- Paper tab

PenFill® cartridge compatible insulin delivery device

-Dose counter
-Dose selector
-Dose selector
-Dose counter
-Dose button

PenFill® cartridge 3 mL (example)

- Threaded end (for needle attachment)
- Colored band
- Rubber plunger

How to use the NovoLog® PenFill® cartridge

- Before you start to prepare your injection, check the NovoLog® PenFill® cartridge label to make sure that it contains the insulin you need. This is especially important if you take more than 1 type of insulin.

- The tamper-resistant foil should be in place before the first use. If the foil has been broken or removed before your first use of the cartridge, do not use it. Call Novo Nordisk at 1-800-727-6500.

- Carefully look at the cartridge and the insulin inside it. Check that the NovoLog® cartridge:
  - is not damaged, for example cracked or leaking
  - is not loose on the threaded end

- NovoLog® should look clear and colorless.

Step 1:

- Insert a 3 mL cartridge with the threaded end first into your Novo Nordisk 3 mL PenFill® cartridge compatible insulin delivery device (See Figure C).

- If you drop your device, check the insulin cartridge for damage such as cracks or leaking. If your cartridge is damaged, throw it away and use a new one.

How to prepare your device with a new needle

Step 2:

- Take a new needle, and tear off the paper tab. Always use a new needle for each injection to make sure the needle is free of germs (sterile) and to prevent blocked needles. Do not attach a new needle to your device until you are ready to give your injection. Do not reuse or share your needles with other people. You may give other people a serious infection, or get a serious infection from them.

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

- Push the needle straight onto the device. Turn the needle clockwise until it is on tight (See Figure D).

Step 3:

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

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

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

Check the insulin flow

Step 5:

- Small amounts of air may collect in the cartridge during normal use. You must do an airshot before each injection to avoid injecting air and to make sure you receive the prescribed dose of your medicine.

- Do the airshot as described in the instruction manual that comes with your device.

- Keep testing your Novo Nordisk 3 mL PenFill® cartridge compatible insulin delivery device until you see insulin at the needle tip. If you still do not see a drop of insulin after 6 times, change the needle and repeat this step. This makes sure that any air bubbles are removed and that insulin is getting through the needle (See Figure G).

Select your dose

Step 6:

- Check to make sure that the dose counter is set to 0.

- Turn the dose selector clockwise to select the dose you need to inject (See Figure H).

- The pointer should line up with your dose. When turning the dose selector, be careful not to press the dose button as insulin will come out. You will hear a click for every single unit dialed. Do not set the dose by counting the number of clicks you hear because you may get an incorrect dose.

- Refer to your insulin delivery device manual if necessary.

Inject your dose

Step 7:

- 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.

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

- For each injection, change (rotate) your injection site within the injection area (See Figure I). You do not use the same injection site for each injection.

- Clean your injection site with an alcohol swab. Let your skin dry. Do not touch this area again before injecting.

- Insert the needle into your skin. Press and hold down the dose button until the dose counter shows “0”. Continue to keep the dose button pressed and keep the needle in your skin and slowly count to 6 (See Figure J).

- Remove the needle from your skin.

You may see a drop of NovoLog® at the needle tip after injecting. This is normal and has no effect on the dose you just received. If blood appears after you take the needle out of your skin, press the injection site lightly with a cotton gauze and cover with an adhesive bandage, if necessary. Do not rub the area.
After your injection
Step 8:
• Lay your outer needle cap on a flat surface. Carefully, lead the needle tip into the outer needle cap without touching the needle (See Figure K) and push the outer needle cap completely on.

• Hold the black cartridge holder on the insulin delivery device and unscrew the needle counterclockwise (See Figure L).
• Throw away (dispose of) the needle in an FDA-cleared sharps container as your healthcare professional has instructed you.
• Put your empty NovoLog® PenFill® cartridge and used needles in a FDA-cleared sharps disposal container right away after use. Do not throw away (dispose of) loose needles and PenFill® cartridges in your household trash.
• If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
  • made of a heavy-duty plastic,
  • can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
  • upright and stable during use, and
  • leak-resistant and properly labeled to warn of hazardous waste inside the container.
• When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. Do not reuse or share your needles or syringes with other people. For more information about the safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal.
• Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. Do not recycle your used sharps disposal container.

Step 9:
• Keep the 3 mL PenFill® cartridge in the device. Do not store your device with a needle attached. This will prevent infection or leakage of insulin and will make sure that you receive the right dose of NovoLog®.
• Put the pen cap on your device after each use to protect the insulin from light (See Figure M).

How should I store my NovoLog® PenFill® cartridge?
• Do not freeze NovoLog®. Do not use NovoLog® if it has been frozen.
• Keep NovoLog® away from heat or light.
• Store the NovoLog® PenFill® cartridge without the needle attached.

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

PenFill® cartridges in use:
• Store the PenFill® cartridge you are currently using in the insulin delivery device at room temperature below 86°F (30°C) for up to 28 days. Do not refrigerate.
• The NovoLog® PenFill® cartridge you are using should be thrown away after 28 days, even if it still has insulin left in it.